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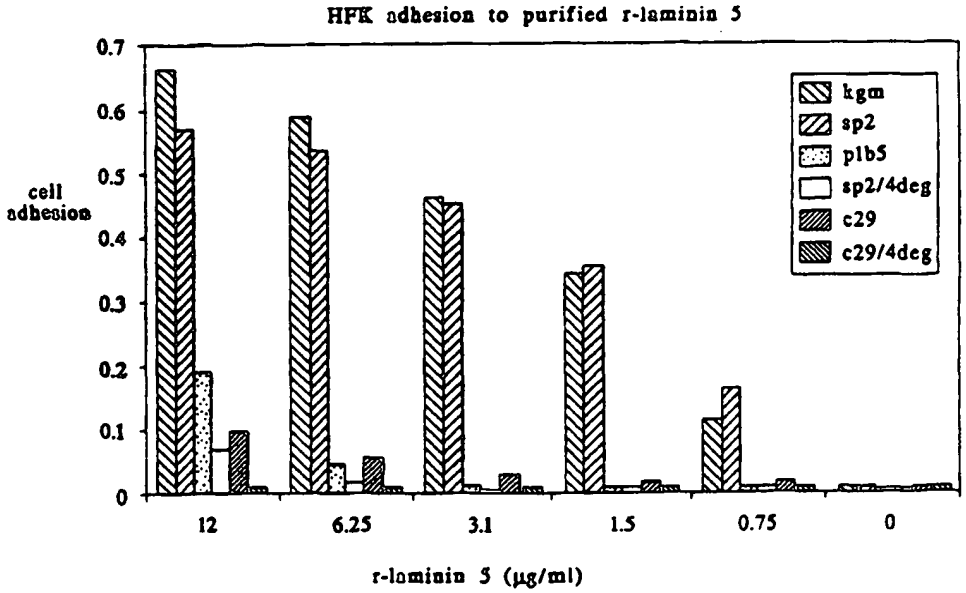

(57) Abstract

The present invention provides recombinant laminin 5, methods for making recombinant laminin 5, cells that express recombinant laminin 5, and methods for using the recombinant laminin 5 to accelerate wound healing, and to promote cell attachment and migration.

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RECOMBINANT LAMININ 5

Cross Reference

This application claims priority to U.S. Provisional Patent Application Serial Nos. 60/131,720 filed April 30, 1999; 60/149,738 filed August 19, 1999; 60/155,945 filed September 24, 1999; and 60/182,012 filed February 11, 2000; all of which are incorporated herein by reference in their entirety.

Field of the Invention

This application relates to recombinant laminin 5 and methods for its use.

Background of the Invention

Basal laminae (basement membranes) are sheet-like, cell-associated extracellular matrices that play a central role in cell growth, tissue development, and tissue maintenance. They are present in virtually all tissues, and appear in the earliest stages of embryonic development.

Basal laminae are central to a variety of architectural and cell-interactive functions. (See for example, Malinda and Kleinman, Int. J. Biochem. Cell Biol. 28:957-959 (1996); Aumailley and Krieg, J. Invest. Dermatology 106:209-214 (1996)):

1. They serve as architectural supports for tissues, providing adhesive substrates for cells.
2. They create perm-selective barriers between tissue compartments that impede the migration of cells and passively regulate the exchange of macromolecules. These properties are illustrated by the kidney glomerular basement membrane, which functions as an important filtration structure, creating an effective blood-tissue barrier that is not permeable to most proteins and cells.
3. Basal laminae create highly interactive surfaces that can promote cell migration and cell elongation during embryogenesis and wound repair. Following an injury, they provide a surface upon which cells regenerate to restore normal tissue function.
4. Basal laminae present information encoded in their structure to contacting cells that is important for differentiation and tissue maintenance. This information is communicated to the cells through various receptors that include the integrins,

dystroglycan, and cell surface proteoglycans. Signaling is dependent not only on the presence of matrix ligands and corresponding receptors that interact with sufficient affinities, but also on such topographical factors as ligand density in a three-dimensional matrix "landscape", and on the ability of basal lamina components to cluster receptors. Because these matrix proteins can be long-lived, basal laminae create a "surface memory" in the basal lamina for resident and transient cells.

The basal lamina is largely composed of laminin and type IV collagen heterotrimers that in turn become organized into complex polymeric structures. To date, six type IV collagen chains and at least twelve laminin chains (and twelve different heterotrimeric laminins) have been identified. These chains possess shared and unique functions and are expressed with specific temporal (developmental) and spatial (tissue-site specific) patterns.

Laminins are a family of heterotrimeric glycoproteins that reside primarily in the basal lamina. They function via binding interactions with neighboring cell receptors, and are important signaling molecules that can strongly influence cellular function. Laminins are important in both maintaining cell/tissue phenotype as well as promoting cell growth and differentiation in tissue repair and development.

Laminins are large, multi-domain proteins, with a common structural organization. The laminin molecule integrates various matrix and cell interactive functions into one molecule.

The laminin molecule is comprised of α-, β-, and γ-chains joined together through a coiled-coil domain. Within this structure are identifiable domains that possess binding activity towards other laminin and basal lamina molecules, and membrane-bound receptors. Domains VI, IVb, and IVa form globular structures, and domains V, IIIb, and IIIa (which contain cysteine-rich EGF-like elements) form rod-like structures. (Kamiguchi et al., Ann. Rev. Neurosci. 21:97-125 (1998)) Domains I and II of the three chains participate in the formation of a triple-stranded coiled-coil structure (the long arm).

Table 1 shows the individual chains that each laminin type is composed of:

TABLE 1. Known laminin family members

Protein	*Chains*
Laminin-1	α1β1γ1

Laminin-2	α2β1γ1
Laminin 3	α1β2γ1
Laminin-4	α2β2γ1
Laminin-5	α3β3γ2
Laminin-6	α3β1γ1
Laminin-7	α3β2γ1
Laminin-8	α4β1γ1
Laminin-9	α4β2γ1
Laminin-10	α5β1γ1
Laminin –11	α5β2γ1
Laminin-12	α2β1γ3

Four structurally-defined family groups of laminins have been identified. The first group of five identified laminin molecules all share the β1 and γ1 chains, and vary by their α-chain composition (α1 to α5 chain). The second group of five identified laminin molecules all share the β2 and γ1 chain, and again vary by their α-chain composition. The third group of identified laminin molecules has one identified member, laminin 5, with a chain composition of α3β3γ2. The fourth group of identified laminin molecules has one identified member, laminin 12, with the newly identified γ3 chain (α2β1γ3)

Some progress has been made in elucidating the relationship between domain structure and function. (See, for example, Wewer and Engvall, Neuromusc. Disord. 6:409-418 (1996).) The overall sequence similarity among the homologous domains in different chains varies, but it is highest in domain VI (thought to play a key role in laminin polymerization), followed by domains V (possibly involved in protein-protein interactions) and III (entactin/nidogen binding; possible cell adhesion sites), and is lowest in domains I, II (both thought to be involved in intermolecular assembly, and containing possible cell adhesion sites), and G. Not all domains are present in all 3 types of chains. The globular G domain (thought to be involved in cell receptor binding) is present only in the α chains. Other domains may not be present in all chains within a certain chain type. For example, domain VI is absent from α3, α4, and γ2 chains. (Wewer and Engvall, 1996)

As a result of their large size (>600 kD) and unique structure, the laminin molecules can be resolved in the electron microscope. (Wewer and Engvall, 1996) Typically, laminins appear as cross-shaped molecules in an EM. The three short arms of the cross represent the amino terminal portions of each of the three separate laminin chains (one short arm per chain). The long arm of the cross is composed of the C-terminal parts of the three chains, which together form a coiled coil structure. (Wewer and Engvall, 1996) The long arm ends with the globular G domain.

The coiled-coil domain of the long arm is crucial for assembly of the three chains of laminin. (Yurchenco et al., Proc. Natl. Acad. Sci. 94:10189-10194 (1997)). Disulfide bonds bridge and stabilize all three chains in the most proximal region of the long arm and join the β and γ chains in the most distal region of the long arm.

A model of laminin receptor-facilitated self-assembly, based on studies conducted with cultured skeletal myotubes and Schwann cells, predicts that laminins bind to their receptors, which freely diffuse in a fluidic membrane, when ligand-free. Receptor engagement forces these receptors into a high local two-dimensional concentration, facilitating their mass-action driven assembly into ordered surface polymers. In this process, the engaged receptors are also reorganized, accompanied by cytoskeletal rearrangements. (Colognato, J. Cell Biol. 145:619-631 (1999)) This reorganization activates the receptors, causing signal transduction with the alteration of cell expression, shape and/or behavior.

One class of laminin receptors are the integrins, which are cell surface receptors that mediate many cell-matrix and cell-cell interactions. Integrins are heterodimers, consisting of an α and a β subunit. 16 α- and 8 β-subunits are known, and at least 22 combinations of α and β subunits have been identified to date. Some integrins have only one or a few known ligands, whereas others appear to be very promiscuous. Binding to integrins is generally of low affinity, and is dependent on divalent cations. Integrins, activated through binding to their ligands, transduce signals via kinase activation cascades, such as focal adhesion and mitogen-activated kinases. Several different integrins bind different laminin isoforms more or less specifically. (Aumailley et al., In The Laminins, Timpl and Ekblom, eds., Harwood Academic Publishers, Amsterdam. pp. 127-158 (1996))

Laminin-5, also referred to as kalinin, nicein, and epiligrin, plays a key role in modulating the behavior and activity of cells and tissues of epithelial origin, and is expected to have broad uses in clinical settings where increased epithelial attachment and hemidesmosome assembly are required. (Takeda et al., J. Invest. Dermatol. 1999 113(1):38-42) Laminin-5 is a principal adhesive ligand in the epidermal basal lamina, and has been shown to promote the attachment of keratinocytes and epithelial cells to the basal lamina and underlying dermis, and also promotes hemidesmosome formation. (Burgeson et al. U.S. Patent No. 5,770,562; Quaranta and Hormia, U.S. Patent No. 5,422,264; Jones, U.S. Patent No. 5,541,106; Quaranta and Hormia, U.S. Patent No. 5,658,789; Hormia et al., J. Invest. Dermatol. 1995 Oct. 105(4):557-561).

Laminin 5 is also thought to be necessary for the healing of epithelial tissue wounds. (Goldfinger et al., J. Cell Sci. 1999; 112(Pt. 16):2615-2629) Pretreatment of human keratinocyte sheets for grafting with laminin 5 improves grafting efficiency. (Takeda et al., J. Invest. Dermatol. 1999 Jul; 113(1):38-42). The addition of laminin-5 accelerates the formation of a basement membrane in a skin equivalent model (Tsunenaga et al., *Matrix Biol.* 17(8-9):603-613, 1998). Laminin-5 also promotes epithelial cell attachment to a wide variety of biomaterials, including polymers, hydroxyapatite, and metals. (Jones et al., U.S. Patent No. 5,585,267; El Ghannam et al., J. Biomed. Mater. Res. 1998 Jul; 41(1):30-40)

Laminin 5 has further been demonstrated to promote the following:

1. Epithelial cell adhesion to the internal basal lamina of teeth (Mullen et al., J. Periodontal. Res. 1999 Jan 34(1):16-24; Hormia et al., J. Dent. Res. 1998 Jul; 77(7):1479-1485) and anchorage of ameloblasts (ie: enamel-producing cells) to the enamel matrix. (Yoshiba et al., Cell Tissue Res. 1998 Apr; 292(1):143-149)

2. Corneal epithelial cell adhesion. (Qin and Kurpakus, Exp. Eye Res. 1998 May 66(5):569-579)

3. Intestinal epithelial restitution. (Lotz et al., Am. J. Pathol. 1997 Feb;150(2):747-760)

4. In vitro expansion of epithelial cells by providing an efficient adhesion substrate for primary cell cultures, thus providing the basis for a wide range of new cell therapy applications. (Gonzales et al., Mol. Biol. Cell. 1999 Feb; 10(2):259-270; Baker et al., Exp. Cell Res. 1996 Nov 1; 228(2)262-270).

5. Proliferation of pancreatic beta islet cells (Todorov et al., Transplant. Proc. 1998 Mar; 30(2): 455; Quaranta and Jones, U.S. Patent No. 5,510,263; Halberstadt et al, U.S. Patent No. 5,681,587; Halberstadt et al., U.S. Patent No. 5,672,361), and T cells (Vivinus-Nebot et al., J. Cell Biol. 1999 Feb 8; 144(3):563-574)

Thus, laminin 5 has broad uses in clinical settings where increased epithelial attachment and hemidesmosome assembly are required. Laminin 5 can be used to promote wound healing and tissue regeneration. The application of exogenous laminin 5 has broad application for the accelerated healing of skin disorders, such as diabetic foot ulcers, venous ulcers, pressure sores, skin surgery, burns, and acute wounds. Exogenous laminin 5 may be used to directly treat a wound surface, or may be applied to a variety of medical devices and dermal grafts for skin, corneal, gastrointestinal, and periodontal epithelial wound healing. The use of laminin 5 provides enhanced biocompatibility of the device or graft, which leads to improved tissue integration and remodeling, reduced immune response, and

reduced likelihood of infection. Laminin 5 is also useful for the ex vivo and in vitro proliferation of various cell types, including but not limited to epithelial cells, pancreatic beta islet cells, and T cells, and tissue equivalents. Thus, a source of laminin 5 for tissue culture media or a media supplement, as well as cell growth substrates coated with laminin 5, would be particularly useful for the cultivation of these and other cell types.

A good source and purification procedure for laminin-5 is needed to provide material for the development of the therapeutic and research applications mentioned above. Some cell lines secrete laminin-5, and procedures have been developed to purify laminin-5 from the processed cells and cell media. However, these methods are time consuming and capable of producing only small amounts of laminin 5. (Rouselle et al., J. Biol. Chem. 1995 270(23):13766-13770; Cheng et al., J. Biol. Chem. 1997, 272(50):31525-31532)

A preferred method of production, however, is the use of recombinant DNA technology to engineer a cell line of choice to produce recombinant laminin-5. A recombinant-based method of laminin-5 production has several advantages over purification from tissue or isolation from cell lines in culture:

1. The recombinant produced protein is free of pathogens. While this is also true for endogenous cell culture produced protein, protein derived from human tissue carries a risk for contamination by HIV, hepatitis, and other infectious agents.

2. Expression levels of the protein, and hence yields, can be improved through the use of genetically engineered genes/vectors that enhance the production of the encoded protein.

3. It is possible to engineer additional peptide sequences to the protein chain that provides a binding site for a commercially viable affinity purification procedure.

4. The method can provide for the modification of protein structure/function through the addition, substitution, elimination, and/or other modifications of protein domain structures. For example, it may be desirable to introduce an integrin binding site (e.g. RGD), switch integrin recognition sites, or engineer in a stable binding site to a synthetic substrate. Thus, the creation of expression vectors that express laminin chains generates enormous flexibility for future uses and creates a basis for creating second generation "designer" laminins.

Previous studies have produced cells transfected with one or two of the laminin 5 chain-encoding DNA sequences, but none have produced recombinant heterotrimeric laminin 5, not have they produced cell lines that secrete recombinant heterotrimeric laminin 5.

(Gagnoux-Palacios et al., J. Biol. Chem. 271:18437-18444 (1996); Matsui et al., J. Biol. Chem. 270:23496-23503 (1995))

Thus, there exists a need in the art for recombinant heterotrimeric laminin 5 protein, methods for making recombinant laminin 5, and methods of using recombinant laminin 5 for wound healing and tissue regeneration, for use on a variety of medical devices and dermal grafts for skin, corneal, gastrointestinal, and periodontal epithelial wound healing, for the ex vivo and in vitro proliferation of various cell types, and for tissue culture media, media supplements, and as a component of cell growth substrates.

Summary of the Invention

The present invention fulfills the need in the art for recombinant laminin 5 protein, methods for making recombinant laminin 5, and methods of using recombinant laminin 5 for the treatment of burns, for use on a variety of medical devices and dermal grafts for skin, corneal, gastrointestinal, and periodontal epithelial wound healing, for the ex vivo and in vitro proliferation of various cell types, and for tissue culture media, media supplements, and as a component of cell growth substrates.

In one aspect, the present invention provides cells that have been transfected with nucleic acid sequences encoding laminin $\alpha 3$, $\beta 3$ and $\gamma 2$ chains, wherein the cells express the individual chains, which assemble into heterotrimeric recombinant laminin-5 (hereinafter referred to as "r-laminin 5"). r-laminin 5, or processed forms thereof, are secreted by the cell.

In another aspect, the present invention provides r-laminin 5, and methods for producing substantially purified r-laminin 5, or processed forms thereof.

In a further aspect, the present invention provides pharmaceutical compositions, comprising r-laminin 5, or processed forms thereof, together with a pharmaceutically acceptable carrier. Such pharmaceutical compositions can optionally be provided with other compounds with wound healing and tissue regeneration utility, such as other extracellular matrix components.

In further aspect, the present invention provides methods and kits for using r-laminin 5 to:

a. accelerate wound healing and tissue regeneration;
b. enhance the performance of skin grafts;
c. improve the attachment of gum tissue to the tooth surface;

d. improve the biocompatibility of medical devices; and

e. accelerate cell proliferation,

by providing an amount effective of r-laminin 5 for the various methods. The invention also provides methods and kits for using laminin 5 to regulate angiogenesis. The kits comprise an amount of laminin 5 or r-laminin 5 effective for the desired effect, and instructions for the use thereof.

In a further aspect, the present invention provides improved medical devices and grafts, wherein the improvement comprises coating the devices or grafts with an amount effective of r-laminin 5 or the pharmaceutical compositions of the invention for the desired application.

In a further aspect, the invention provides improved cell culture devices for the proliferation of cells in culture, by providing an amount effective of r-laminin 5 for the attachment of cells to a cell culture device for the attachment and subsequent proliferation, differentiation, or maintenance of the cells.

In another aspect, the invention provides a cell culture growth supplement, comprising r-laminin 5. In another aspect, the invention provides an improved cell culture growth media, wherein the improvement comprises the addition of r-laminin 5.

Brief Description of the Figures

Figure 1 is a bar graph showing the results of an HFK cell adhesion assay for r-laminin 5 activity in culture media from various clones.

Figure 2 is a bar graph showing a cell adhesion assay in which r-laminin 5 was coated directly onto the plate. p1b5 = anti-integrin $\alpha 3\beta 1$ antibody; sp2 = control IgG, non-specific; C29: anti-laminin 5 antibody

Figure 3 is a rotary shadow analysis of r-laminin 5. Purified r-laminin 5 protein was diluted to 50 μg/ml and adjusted to 70% glycerol/30% 0.15M ammonium bicarbonate and rotary shadowed using standard techniques. An approximately 80,000X magnification field is shown of (A) r-laminin 5; (B) "native" laminin 5 (purified by BM165 monoclonal antibody affinity chromatography from SCC-25 (squamous cell carcinoma cell line) conditioned medium). The bar represents 50 nm.

Detailed Description of the Preferred Embodiments

All references, patents and patent applications are hereby incorporated by reference in their entirety.

Within this application, unless otherwise stated, the techniques utilized may be found in any of several well-known references such as: *Molecular Cloning: A Laboratory Manual* (Sambrook, et al., 1989, Cold Spring Harbor Laboratory Press), *Gene Expression Technology* (Methods in Enzymology, Vol. 185, edited by D. Goeddel, 1991. Academic Press, San Diego, CA), "Guide to Protein Purification" in *Methods in Enzymology* (M.P. Deutshcer, ed., (1990) Academic Press, Inc.); *PCR Protocols: A Guide to Methods and Applications* (Innis, et al. 1990. Academic Press, San Diego, CA), *Culture of Animal Cells: A Manual of Basic Technique, 2nd Ed.* (R.I. Freshney. 1987. Liss, Inc. New York, NY), *Gene Transfer and Expression Protocols*, pp. 109-128, ed. E.J. Murray, The Humana Press Inc., Clifton, N.J.), and the Ambion 1998 Catalog (Ambion, Austin, TX).

As used herein "laminin 5" encompasses both r-laminin 5 and heterotrimeric laminin 5 from naturally occurring sources.

The term "r-laminin 5" refers to include recombinant heterotrimeric laminin 5 expressed by a cell that has been exogenously transfected with expression vector(s) comprising polynucleotides that encode α3, β3 and γ2 laminin polypeptide chains, or a portion of each of the chains which are capable of forming a heterotrimeric laminin 5, as well as versions thereof resulting from cellular processing events. Such r-laminin 5 can comprise α3, β3, and γ2 sequences from a single organism, or from different organisms. Laminin 5 chain DNA sequences and their encoded proteins from a variety of organisms are known in the art. (See, for example, Gerecke et al., J. Biol. Chem. 269:11073-11080 (1994); Kallunki et al., J. Cell Biol. 119:679-693 (1992); Ryan et al., J. Biol. Chem. 269:22779-22787 (1994); Iivananinen et al., J. Biol. Chem. 274:14107-14111 (1999); Galliano et al., J. Biol. Chem. 270:21820-221826 (1995); Sugiyama et al., Eur. J. Biochem. 228:120-128 (1995) all references incorporated by reference herein in their entirety).

In the present invention, r-laminin 5 is a secreted protein, which is capable of being directed to the ER, secretory vesicles, and the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Such processing event can be variable, and thus may yield different versions of the final "mature

protein". The substantially purified r-laminin 5 of the present invention includes heterotrimers comprising both the full length and any such processed laminin 5 chains.

As used herein, the term "substantially purified" means that the recombinant laminin 5 so designated has been separated from its in vivo cellular environments.

As used herein, a laminin 5 polypeptide chain refers to a polypeptide chain according to one or more of the following:

(a) comprises a polypeptide structure selected from the group consisting of:

1. R1-R2-R3
2. R1-R2-R3(e)
3. R3
4. R3(e)
5. R1-R3
6. R1-R3(e)
7. R2-R3
8. R2-R3(e)

wherein R1 is a amino terminal methionine; R2 is a signal sequence that is capable of directing secretion of the polypeptide, wherein the signal sequence may be the natural signal sequence for the particular laminin chain, that of another secreted protein, an artificial sequence; R3 is a secreted laminin chain selected from the α3, β3, and γ2 chains; and R3(e) is a secreted laminin chain selected from the α3, β3, and γ2 chains that further comprises an epitope tag (such as those described below), which can be placed at any position within the laminin chain amino acid sequence; and/or

(b) is encoded by a polynucleotide that is substantially similar to the disclosed laminin polynucleotide sequences or portions thereof (SEQ ID NOS.: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35); and/or

(c) is encoded by a polynucleotide that hybridizes under high or low stringency conditions to coding regions, or portions thereof, of one or more of the recombinant laminin 5 chain DNA sequences disclosed herein (SEQ ID NOS.: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35), or complementary sequences thereof; and/or

(d) has at least 70% identity to the disclosed laminin polypeptide claim amino acid sequences (SEQ ID NOS.: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36), preferably at least 80% identity, and most preferably at least about 90% identity.

The phrase "substantially similar" is used herein in reference to polynucleotide or polypeptide sequences having one or more conservative variations from the laminin 5 sequences disclosed herein, including but not limited to deletions, insertions, inversions, repeats, and substitutions, wherein the resulting laminin chain is functionally equivalent to those disclosed herein.

For example, conservative polynucleotide variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, including but not limited to optimizing codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

Naturally occurring conservative variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level. Alternatively, non-naturally occurring conservative variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, conservative polynucleotide variants may be generated to improve or alter the characteristics of the expressed laminin chain polypeptides. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the secreted protein. (See, for example, Ron et al., J. Biol. Chem. 268: 2984-2988 (1993); Dobeli et al., J. Biotechnology 7:199-216 (1988)) Ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. (See, for example, Gayleet al., J. Biol. Chem 268:22105-22111 (1993)) Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained.

Guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie, J. U. et al., Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different

species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

The "substantially similar" polypeptides of the present invention also include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group; (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol); and/or (iv) fusion of the polypeptide with additional amino acids, such as an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity.

(Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

"Stringency of hybridization" is used herein to refer to conditions under which nucleic acid hybrids are stable. The invention also includes nucleic acids that hybridize under high stringency conditions (as defined herein) to all or a portion of the coding sequences of the laminin chain polynucleotides disclosed herein, or their complements. The hybridizing portion of the hybridizing nucleic acids is typically at least 50 nucleotides in length. As known to those of skill in the art, the stability of hybrids is reflected in the melting temperature (T_M) of the hybrids. T_M decreases approximately 1-1.5°C with every 1% decrease in sequence homology. In general, the stability of a hybrid is a function of sodium ion concentration and temperature. Typically, the hybridization reaction is performed under conditions of lower stringency, followed by washes of varying, but higher, stringency. Reference to hybridization stringency relates to such washing conditions. Thus, as used herein, high stringency refers to an overnight incubation at 42° C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65°C.

Also contemplated are laminin 5-encoding nucleic acid sequences that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH_2PO_4; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50°C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

As used herein, "percent identity" of two amino acids or of two nucleic acids is determined using the algorithm of Karlin and Altschul (Proc. Natl. Acad. Sci. USA 87:2264-2268, 1990), modified as in Karlin and Altschul (Proc. Natl. Acad. Sci. USA 90:5873-5877, 1993). Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul et al. (J. Mol. Biol. 215:403-410, 1990). BLAST nucleotide searches are performed with the NBLAST program, score = 100, wordlength = 12, to obtain nucleotide sequences homologous to the nucleic acid molecules of the invention. BLAST protein searches are performed with the XBLAST program, score = 50, wordlength = 3, to obtain an amino acid sequence homologous to a polypeptide of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST is utilized as described in Altschul et al. (Nucleic Acids. Res. 25:3389-3402, 1997). When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) are used. See http://www.ncbi.nlm.nih.gov.

Further embodiments of the present invention include polynucleotides encoding laminin chain polypeptides having at least 70% identity, preferably at least 80% identity, and most preferably at least 90% identity to one or more polypeptide sequences, or fragments thereof, contained in SEQ ID NO:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34.

As used herein, "α3 polynucleotide" refers to polynucleotides encoding an α3 laminin chain of the same name. Such polynucleotides can be characterized by one or more of the following: (a) the nucleotides of said polynucleotide may encode an amino acid sequence substantially similar to one or more of the sequences set forth in SEQ ID NO: 2, 4, 6, 8, 10,12 or fragments thereof, or fragments thereof; (b) polynucleotides that encode polypeptides which share at least 70% identity, preferably 80% identity, and most preferably at least 90% identity with one or more of the sequences set forth in SEQ ID NO: 2, 4, 6, 8, 10, 12 or fragments thereof; (c) the α3 polynucleotides hybridize under low or high stringency conditions to the coding sequence set forth in one or more of SEQ ID NO: 1, 3, 5, 7, 9, 11, fragments thereof, or complementary sequences thereof; (d) the α3 polynucleotides may encode a polypeptide with a general structure selected from (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e); wherein R1 and R2 are as described above, and R3 and R3(e) are as described above but comprise secreted α3 chain polypeptides.

As used herein, "β3 polynucleotide" refers to polynucleotides encoding a β3 laminin chain of the same name. Such polynucleotides can be characterized by one or more of the following: (a) the nucleotides of said polynucleotide may encode an amino acid sequence substantially similar to one ore more of the sequences set forth in SEQ ID NO: 14, 16, 18, 20, 22, 24, or fragments thereof; (b) polynucleotides that encode polypeptides which share at least 70% identity, preferably at least 80%, and most preferably at least 90% identity with one or more of the sequences set forth in SEQ ID NO: 14, 16, 18, 20, 22, 24, or fragments thereof; (c) the β3 polynucleotides hybridize under low or high stringency conditions to the coding sequence of one or more of the sequences set forth SEQ ID NO: 13, 15, 17, 19, 21, 23, fragments thereof or complementary sequences thereof; (d) the β3 polynucleotides may encode a polypeptide with a general structure selected from (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e); wherein R1 and R2 are as described above, and R3 and R3(e) are as described above but comprise secreted β3 chain polypeptides.

As used herein, "γ2 polynucleotide" refers to polynucleotides encoding a γ2 laminin chain of the same name. Such polynucleotides can be characterized by one or more of the following: (a) the nucleotides of said polynucleotide may encode an amino acid that is substantially similar to one or more of the sequences set forth in SEQ ID NO: 26, 28, 30, 32, 34, 36 or fragments thereof; (b) polynucleotides that encode polypeptides which share at least 70% identity, preferably at least 80%, and most preferably at least 90% identity with one or more of the sequences set forth in SEQ ID NO: 26, 28, 30, 32, 34, 36 or fragments thereof; (c) the γ2 polynucleotides hybridize under low or high stringency conditions to the coding sequence set forth in one or more of SEQ ID NO: 25, 27, 29, 31, 33, 35, fragments thereof, or complementary sequences thereof; (d) the γ2 polynucleotides may encode a polypeptide with a general structure selected from (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e); wherein R1 and R2 are as described above, and R3 and R3(e) are as described above but comprise secreted γ2 chain polypeptides.

As used herein, the term "epitope tag" refers to a polypeptide sequence that is expressed as part of a chimeric protein, where the epitope tag serves as a recognition site for binding of antibodies generated against the epitope tag, or for binding of other molecules that can be used for affinity purification of sequences containing the tag.

As used herein, the term "increased biocompatibility" refers to reduced induction of acute or chronic inflammatory response, and reduced disruption of the proper differentiation

of implant-surrounding tissues for laminin 5-coated biomaterials relative to an analogous, non-coated biomaterial.

As used herein the term "graft" refers to both natural and prosthetic grafts and implants.

In one aspect, the present invention provides cells that have been systematically transfected with recombinant expression vectors comprising promoter sequences that are operatively linked to polynucleotide sequences encoding polypeptide sequences comprising α3, β3, and γ2 laminin 5 chains. After the multiple transfections, the cells express each of the recombinant laminin 5 chains, which assemble into a heterotrimer and can be purified from the cell culture medium.

In a preferred embodiment, cDNAs encoding proteins comprising the α3, β3, and γ2 laminin polypeptide chains, or fragments thereof, are subcloned into an expression vector. Alternatively, laminin 5 α3, β3, and/or γ2 gene sequences, including one or more introns, and including various 5' and 3' non-coding regions, can be used.

Any cell capable of expressing and secreting the r-laminin 5 can be used. Preferably, eukaryotic cells are used, and most preferably mammalian cells are used, including but not limited to kidney and epithelial cell lines. Especially preferred are those mammalian cells that do not endogenously express laminin 5. Carbohydrate and disulfide post-translational modifications are believed to be required for laminin 5 protein folding and function. This makes the use of eukaryotic cells preferable for producing functional r-laminin 5, although other systems are useful for obtaining, for example, antigens for antibody production.

"Recombinant expression vector" includes vectors that operatively link a nucleic acid coding region or gene to any promoter capable of effecting expression of the gene product. The promoter sequence used to drive expression of the laminin 5 individual chains may be constitutive (driven by any of a variety of promoters, including but not limited to, CMV, SV40, RSV, actin, EF) or inducible (driven by any of a number of inducible promoters including, but not limited to, tetracycline, ecdysone, steroid-responsive). The expression vector must be replicable in the host organisms either as an episome or by integration into host chromosomal DNA. In a preferred embodiment, the expression vector comprises a plasmid. However, the invention is intended to include other expression vectors that serve equivalent functions, such as viral vectors.

In one embodiment, at least one of the laminin chain polypeptide sequences, or fragments thereof, is operatively linked to a nucleic acid sequence encoding an "epitope tag",

so that at least one of the chains is expressed as a fusion protein with an expressed epitope tag. The epitope tag may be expressed as the amino terminus, the carboxy terminus, or internal to the end of a r-laminin 5 chain, so long as the resulting heterotrimeric r-laminin 5 remains functional. Any epitope tag may be utilized, so long as it can be used as the basis for affinity purification of the resulting r-laminin 5 heterotrimer. Examples of such epitope tags include, but are not limited to FLAG (Sigma Chemical, St. Louis, MO), myc (9E10) (Invitrogen, Carlsbad, CA), 6-His (Invitrogen; Novagen, Madison, WI), and HA (Boehringer Manheim Biochemicals).

In another embodiment, one of the r-laminin 5 chains is expressed as a fusion protein with a first epitope tag, and at least one other r-laminin chain is expressed as a fusion protein with a second epitope tag. This permits multiple rounds of purification to be carried out. Alternatively, the same epitope tag can be used to create fusion proteins with more than one of the r-laminin chains.

In a further embodiment, the epitope tag can be engineered to be cleavable from the r-laminin 5 chain(s). Alternatively, no epitope tag is fused to any of the r-laminin 5 chains, and the r-laminin 5 is purified by standard chromatography techniques, including but not limited to affinity chromatography using laminin 5 specific antibodies or other laminin 5 binding molecules, ionic exchange, hydrophobic exchange, etc.

Transfection of expression vectors into the host cells can be accomplished via any technique known in the art, including but not limited to standard bacterial transformation, calcium phosphate co-precipitation, electroporation, or liposome mediated-, DEAE dextran mediated-, polycationic mediated-, or viral mediated transfection.

In a preferred embodiment, the cells are stably transfected. Any methods for stable transfection and selection of appropriate transfected cells are known in the art. In a most preferred embodiment, a CMV promoter driven expression vector is used in a human kidney embryonic 293 cell line.

Media from cells transfected with a single laminin chain are initially analyzed on Western blots using chain-specific anti-laminin-5 antibodies. The expression of single laminin chains following transfection is generally intracellular. Clones showing reactivity against individual transfected chain(s) are verified by any appropriate method, such as PCR, reverse transcription-PCR, or nucleic acid hybridization, to confirm incorporation of the transfected gene. Preferably, analysis of genomic DNA preparations from such clones is done by PCR using laminin chain-specific primer pairs. Media from transfected clones producing all three chains are further analyzed for heterotrimeric laminin 5 secretion and/or

activity, by any appropriate method, including Western blot analysis and cell binding assays, such as a keratinocyte cell adhesion assay.

In another aspect, the present invention provides substantially purified r-laminin 5, comprising an α3 chain, a β3 chain, and a γ2 chain, and methods for producing substantially purified r-laminin 5. In one embodiment, the r-laminin 5 comprises a first chain comprising a polypeptide that is substantially similar to at least one of the sequences shown in SEQ ID NO:2, 4, 6, 8, 10, 12 or fragments thereof; a second chain comprising a polypeptide that is substantially similar to at least one of the sequences shown in SEQ ID NO:14, 16, 18, 20, 22, 24, or fragments thereof; and a third chain comprising a polypeptide that is substantially similar to at least one of the sequences shown in SEQ ID NO:26, 28, 30, 32, 34, 36, or fragments thereof, wherein the first, second, and third polypeptides are produced recombinantly, and wherein the first, second, and third chains assemble into a recombinant heterotrimeric laminin 5.

In another embodiment, the substantially purified r-laminin 5 comprises a first chain comprising a polypeptide that is at least about 70% identical to at least one of the sequences shown in SEQ ID NO:2, 4, 6, 8, 10, 12, or fragments thereof; a second chain comprising a polypeptide that is at least 70% identical to at least one of the sequences shown in SEQ ID NO:14, 16, 18, 20, 22, 24, or fragments thereof; and a third chain comprising a polypeptide that is at least 70% identical to at least one of the sequences shown in SEQ ID NO:26, 28, 30, 32, 34, 36, or fragments thereof, wherein the first, second, and third polypeptides assemble into a recombinant heterotrimeric laminin 5.

In a preferred embodiment, at least one of the first, second, or third chains of the substantially purified human r-laminin 5 is expressed as a fusion protein with an epitope tag.

Alternatively, the r-laminin 5 comprises a heterotrimeric polypeptide structure, wherein each individual chain comprises a general structure selected from the group consisting of: (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e)

wherein R1 is a amino terminal methionine; R2 is a signal sequence that is capable of directing secretion of the polypeptide, wherein the signal sequence may be the natural signal sequence for the particular laminin chain, that of another secreted protein, or an artificial sequence; R3 is a secreted α3, β3, or γ2 laminin chain; and R3(e) is a secreted laminin α3, β3, and γ2 chain that further comprises an epitope tag (such as those described above), which can be placed at any position within the laminin chain amino acid sequence.

In a preferred embodiment, purification of the r-laminin 5 is accomplished by passing media from the transfected cells through an affinity column. For example, antibodies or other binding molecules that bind to a peptide epitope expressed on at least one of the recombinant chains are attached to an affinity column, and bind r-laminin 5 that has been secreted into the media. The r-laminin 5 is removed from the column by passing excess peptide through the column. The eluted protein can subsequently be further purified, if desired.

Eluted fractions are analyzed by any appropriate method, including gel electrophoresis and Western blot analysis. In a further embodiment, the peptide epitope can be cleaved after purification. In other embodiments, two or three separate r-laminin chains are expressed as fusion proteins, each with a different epitope tag, permitting two or three rounds of purification and a doubly or triply purified r-laminin 5. The epitope tag can be engineered so as to be cleavable from the r-laminin 5 chain(s) after purification. Alternatively, no epitope tag is fused to any of the r-laminin 5 chains, and the r-laminin 5 is purified by standard techniques, including but not limited to affinity chromatography using laminin 5 specific antibodies or other laminin 5 binding molecules.

In another aspect, the present invention provides novel laminin β3 and γ2 chain nucleic acids and proteins, consisting of the nucleic acid sequences and proteins disclosed as SEQ ID NO:21-22, 23-24, 29-30, and 31-32.

The present invention further provides pharmaceutical compositions comprising r-laminin 5, as disclosed above, and a pharmaceutically acceptable carrier. According to this aspect of the invention, other agents can be included in the pharmaceutical compositions, depending on the condition being treated, including but not limited to any of the collagens, other laminin types, fibronectin, integrins, glycoproteins, proteoglycans, heparan and heparan sulfate proteoglycans, growth factors such as vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF), and keratinocyte growth factor (KGF); glycosaminoglycans, entactin, nidogen, and peptide fragments thereof.

Pharmaceutical preparations comprising r-laminin 5 can be prepared in any suitable form, and generally comprise the r-laminin 5 in combination with any of the well known pharmaceutically acceptable carriers. The carriers can be injectable carriers, topical carriers, transdermal carriers, and the like. The preparation may advantageously be in a form for topical administration, such as an ointment, gel, cream, spray, dispersion, suspension or paste. The preparations may further advantageously include preservatives, antibacterials, antifungals, antioxidants, osmotic agents, and similar materials in composition and quantity

as is conventional. Suitable solutions for use in accordance with the invention are sterile, are not harmful for the proposed application, and may be subjected to conventional pharmaceutical operations such as sterilization and/or may contain conventional adjuvants, such as preservatives, stabilizers, wetting agents, emulsifiers, buffers etc. For assistance in formulating the compositions of the present invention, one may refer to Remington's Pharmaceutical Sciences, 15th Ed., Mack Publishing Co., Easton, Pa. (1975).

The dosage regimen for various treatments using the r-laminin 5 of the present invention is based on a variety of factors, including the type of injury or condition, the age, weight, sex, medical condition of the individual, the severity of the condition, and the route of administration. Thus, the dosage regimen may vary widely, but can be determined routinely by a physician using standard methods. Laminins are extremely potent molecules, and one or a few molecules per cell could produce an effect. Thus, effective doses in the pico-gram per milliliter range are possible if the delivery is optimized. Laminins are sometimes present in an insoluble form in the basement membrane and have the capability of polymerizing at concentrations ranging as low as about 50 μg/ml, depending on the laminin isoform and the conditions. Laminins can also polymerize into a gel at a concentration of 2-3 mg/ml. Dosage levels of the order of between 1 ng/ml and 10 mg/ml are thus useful for all methods disclosed herein, preferably between about 1 μg/ml and about 3 mg/ml.

The treatment regime will also vary depending on the condition of the subject, based on a variety of factors, including the type of injury, the age, weight, sex, medical condition of the individual, the severity of the condition, and the route of administration. For example, r-laminin 5 can be used to coat a wound dressing, which is placed in contact with a patient's wound as frequently as the dressing needs to be changed, and for as long as the dressing is applied to the wound surface.

Similarly, the route of administration will vary depending on the condition of the subject, based on a variety of factors, including the type of injury, the age, weight, sex, medical condition of the individual, and the severity of the condition.

In further aspect, the present invention provides methods for using r-laminin 5, or the pharmaceutical compositions of the invention, to accelerate wound healing and tissue regeneration. In preferred embodiments, r-laminin 5 is used to accelerate the healing of skin in diabetic foot ulcers, venous ulcers, pressure sores, skin surgery, severe burns, and acute wounds, and enhanced performance of skin grafts (both autologous and artificial). In another aspect, the present invention provides kits for carrying out these methods, comprising an

amount effective of laminin 5 or r-laminin 5 and instructions for using the laminin 5 to carry out the methods.

In one embodiment, r-laminin 5, or a pharmaceutical composition comprising r-laminin 5, is used to enhance wound healing by promoting the adhesion of transplanted cultured keratinocytes or other epithelial cells to an underlying substrate, such as a mammalian or human dermis. The substrate may comprise a wound surface, the basal surface of a confluent layer of cultured epithelial cells to be transplanted, or a substrate to be applied to the wound surface, such as a wound dressing, prior to placing the layer on a graft site. The r-laminin 5 may be supplied in a pharmaceutically acceptable carrier, preferably in amounts of between about 1 ng/ml and about 10 mg/ml.

The use of kalinin-containing (ie: laminin 5-containing) isolated cell matrices has previously been shown to enhance the adhesion of transplanted cultured keratinocytes to an underlying substrate (Burgeson et al., US Patent No. 5,770,562). This and other studies have thus demonstrated that laminin 5 stimulates epithelial cell attachment and spreading, and thus provides an appropriate surface facilitating the healing of skin and the use of skin grafts. (Quaranta and Hormia, U.S. Patent No. 5,422,264; Jones, U.S. Patent No. 5,541,106; Quaranta and Hormia, U.S. Patent No. 5,658,789; Hormia et al., J. Invest. Dermatol. 1995 Oct. 105(4):557-561; Takeda et al., J. Invest. Dermatol. 1999 Jul; 113(1):38-42; Goldfinger et al., J. Cell Sci. 1999; 112(Pt. 16):2615-2629).

Thus, the addition of r-laminin 5 to the appropriate injured tissue can promote cell growth, cell migration, and accelerate tissue regeneration. Accelerated healing has the added benefit of reducing inflammatory responses and scarring. This can be accomplished in some cases by simply coating the r-laminin 5 or the pharmaceutical compositions of the invention into a wound area (such as skin, periodontal epithelial cells), or in other cases, by providing a suitable substrate to which r-laminin 5 has been anchored, including but not limited to wound dressing and matrices, graft substrates, and dental abutments.

The incorporation of recombinant r-laminin 5 into wound repair dressings and matrices as well as tissue grafts will provide a natural ligand interactive surface to promote normal cell adherence, cell growth and tissue development. Many grafts are used to replace tissue that has an epithelial cell layer adherent to a basal lamina. When an inappropriate surface is provided to these cells following grafting, the graft is at risk for failure of restoration of the normal cell layer. The advantage of coating these grafts with r-laminin 5 is to create a surface that sufficiently recapitulates a normal basal lamina surface to promote cell re-population.

Skin grafts are used in cases were large surface areas of skin have been burned or injured. The application of r-laminin 5 and/or the pharmaceutical compositions of the invention will significantly promote the attachment and 'take' of skin grafts to the injured tissue, as well as promote normal skin healing processes while minimizing scar tissue formation.

Collagen-based matrices are also applied to serious skin injuries to promote the growth of the underlying dermis and improve the take of a skin graft. Coating the collagen matrices with r-laminin-5 will create a more natural ligand interactive surface to promote cell migration, cell proliferation and the regeneration of the dermis. An acceleration of the regeneration of the dermis, and take of the skin graft, will minimize scar tissue formation.

Purified laminin 5 has been demonstrated to support epithelial cell adhesion to the internal basal lamina of teeth (Mullen et al., J. Periodontal. Res. 1999 Jan 34(1):16-24; Hormia et al., J. Dent. Res. 1998 Jul; 77(7):1479-1485) and is believed to strengthen the anchorage of ameloblasts (ie: enamel-producing cells) to the enamel matrix. (Yoshiba et al., Cell Tissue Res. 1998 Apr; 292(1):143-149). Thus, in another embodiment, the r-laminin 5 or the pharmaceutical compositions of the invention are used to stimulate epithelium cell adhesion to the internal basal lamina of teeth and of ameloblasts to the enamel matrix of teeth. Such treatments are useful for the treatment of periodontal diseases, including but not limited to oral ulcerations, gingivitis and periodontitis. For example, existing teeth may be coated with the r-laminin 5 or the pharmaceutical compositions of the present invention as a treatment for gum (junctional epithelium) diseases, including but not limited to gingivitis and periodontitis, which promote the detachment of the gum from the tooth. These disease conditions allow the accumulation of food and other foreign matter in the space between the gum and the tooth, resulting in infection. The r-laminin 5 will promote reattachment of the gum to the tooth, thus preventing entry of foreign matter and subsequent infection.

For use in treating gingivitis and other periodontal diseases and disorders, the pharmaceutical compositions of the present invention may be in the form of toothcreams, toothpastes, liquid dentifrices, tooth-powders chewing-gum, tablets and the like. The pharmaceutical compositions of the invention can also contain flavoring, coloring agents, sweeteners, preservatives, surface active agents, and the like.

Purified laminin-5 has been shown to promote the *in vitro* expansion of epithelial cells (Gonzales et al., Mol. Biol. Cell. 1999 Feb; 10(2):259-270; Baker et al., Exp. Cell Res. 1996 Nov 1; 228(2)262-270), pancreatic beta islet cells (Todorov et al., Transplant. Proc. 1998 Mar; 30(2): 455; Quaranta and Jones, U.S. Patent No. 5,510,263; Halberstadt et al, U.S.

Patent No. 5,681,587; Halberstadt et al., U.S. Patent No. 5,672,361), and T cells (Vivinus-Nebot et al., J. Cell Biol. 1999 Feb 8; 144(3):563-574), by providing an efficient adhesion substrate for primary cell cultures. Thus, in another aspect of the present invention, r-laminin 5 is used to enhance the adhesion of cells for proliferation, differentiation, or maintenance of cells including, but not limited to pancreatic beta islet cells, epithelial cells, or T cells, by contacting the cells with an amount effective of r-laminin 5 to provide an efficient adhesion substrate for attachment and subsequent proliferation, differentiation, or maintenance of the cells. The r-laminin 5 can be provided in the cell culture medium, as a cell culture medium supplement, or may be coated on the surface of a cell growth substrate. In each case, r-laminin 5 is preferably used at a concentration of between about 1 ng/ml and about 10 mg/ml. The cells can optionally be contacted with other compounds that promote cell adhesion, proliferation, differentiation, and/or maintenance, including but not limited to any of the collagens, other laminin types, fibronectin, integrins, glycoproteins, proteoglycans, heparan sulfate proteoglycan, glycosaminoglycans, entactin, nidogen, and peptide fragments thereof.

The cells may be primary cells or cell lines. The methods of this aspect of the invention can be used in vivo, ex vivo, or in vitro.

In a preferred embodiment, r-laminin 5 is used to coat the surface of a substrate to promote cell adhesion to the substrate, and to stimulate cell proliferation, differentiation, and/or maintenance. The substrate used herein may be any desired substrate. For laboratory use, the substrate may be as simple as glass or plastic. For use in vivo, the substrate may be any biologically compatible material capable of supporting cell growth. Suitable substrate materials include shaped articles made of or coated with such materials as collagen, regenerated collagen, polyglycolic acid, polygalactose, polylactic acid or derivatives thereof; biocompatible metals such as titanium and stainless steel; ceramic materials including prosthetic material such as hydroxylapatite; synthetic polymers including polyesters and nylons; polystyrene; polyacrylates; polytetrafluoroethylene, and virtually any other material to which biological molecules can readily adhere. The determination of the ability of a particular material to support adhesion of r-laminin 5 of the invention requires only routine experimentation by the skilled artisan.

In a further aspect, the present invention provides a method of treating Type I diabetes in a patient in need thereof comprising contacting pancreatic beta islet cells with an amount effective of r-laminin 5 to provide an efficient adhesion substrate for the cells, leading to increased proliferation of insulin-producing pancreatic beta islet cells, and administering the cells to a patient in need thereof.

Nearly two million Americans are afflicted with Type I (insulin-dependent) diabetes, in which the pancreas has lost its ability to secrete insulin due to an autoimmune disorder in which the insulin-secreting beta cells, found within the islet cells of the pancreas, are destroyed. Although insulin injections can compensate for beta cell destruction, blood sugar levels can still fluctuate dramatically. The impaired ability to take up glucose from the blood results in side reactions in which toxic products accumulate, leading to complications including blindness, kidney disease, nerve damage, and, ultimately, coma and death.

(U.S. Patent No. 5,672,361)

The pancreatic beta islet cells to be grown are plated on or applied to the matrix-coated substrate using standard tissue culture techniques, followed by expansion in standard cell growth medium (as disclosed in U.S. Patent No. 5,672,361) in the presence of r-laminin 5. Any medium capable of supporting the enhanced growth of adult islet cells on the matrix-coated substrate is within the scope of the invention, as discussed above.

Fetal pancreatic islet cells may be grown in vitro in the presence of r-laminin 5 for transplantation into diabetic patients. Growth of fetal pancreatic islet cells in the presence of r-laminin 5 increases the yield of islet cells for transplantation and thus solves the need to produce larger amounts of these cells. In addition, it is contemplated that the inclusion of other growth factors in the adult islet cell culture medium will further increase the yield of islet cells.

Laminins, or cell extracts containing laminins have been shown to regulate angiogenesis in a biphasic manner. (See, for example, Nicosia et al., Dev. Biol. 164:197-206 (1994); Bonfil et al., Int. J. Cancer 58:233-239 (1994)). At lower concentrations (30-300 μg/ml), a laminin-entactin complex stimulated angiogenesis in a three-dimensional culture, while at 3000 μg/ml the same complex was inhibitory to angiogenesis. Thus, in another aspect, the present invention provides methods for regulating angiogenesis, comprising contacting a tissue or culture substrate with an amount effective of laminin 5 or pharmaceutical compositions thereof to regulate angiogenesis. In one embodiments, the laminin 5 is used to promote angiogenesis by contacting a tissue or culture substrate with an amount effective of laminin 5 to promote angiogenesis. In another embodiment, the laminin 5 is used to inhibit angiogenesis, by contacting the tissue or culture substrate with an amount effective of laminin 5 to inhibit angiogenesis. An example of culture substrates to be contacted with laminin 5 to regulate angiogenesis are those used for tissue engineering purposes.

As used herein, the term "angiogenesis" refers to the formation of blood vessels. Specifically, angiogenesis is a multistep process in which endothelial cells focally degrade and invade through their own basement membrane, migrate through interstitial stroma toward an angiogenic stimulus, proliferate proximal to the migrating tip, organize into blood vessels, and reattach to newly synthesized basement membrane (see Folkman et al., Adv. Cancer Res., Vol. 43, pp. 175-203 (1985)). Compounds that promote angiogenesis can be used to promote wound healing and skin grafting, organ transplantation (including artificial organs), acceleration of endothelial cell coverage of vascular grafts to prevent graft failure due to re-occlusion, to treat ischemic conditions, and to treat inflammatory diseases.

In a further aspect, the present invention provides cell substrates comprising an amount effective of r-laminin 5 for the adhesion, growth, or maintenance of cells in culture,. The substrates may comprise any of the substrates discussed above. Preferably, the r-laminin 5 is coated on the surface of the substrate using solution at a concentration of between about 1 ng/ml and about 10 mg/ml.

In another aspect of the present invention, an improved cell culture medium is provided, wherein the improvement comprises addition to the cell culture medium of an effective amount of r-laminin 5 to the cell culture medium to promote the adherence, proliferation, and/or maintenance of cells. Any cell culture media that can support the growth of cells can be used with the present invention. Such cell culture media include, but are not limited to Basal Media Eagle, Dulbecco's Modified Eagle Medium, Iscove's Modified Dulbecco's Medium, McCoy's Medium, Minimum Essential Medium, F-10 Nutrient Mixtures, Opti-MEM® Reduced-Serum Medium, RPMI Medium, and Macrophage-SFM Medium or combinations thereof.

The improved cell culture medium can be supplied in either a concentrated (ie: 10X) or non-concentrated form, and may be supplied as either a liquid, a powder, or a lyophilizate. The cell culture may be either chemically defined, or may contain a serum supplement. Culture media is commercially available from many sources, such as GIBCO BRL (Gaithersburg, MD) and Sigma (St. Louis, MO). Alternatively, the r-laminin 5 is used as a cell culture supplement, and can be separately added to the cell culture medium.

Purified laminin-5 has also been shown to promote epithelial cell attachment to a wide variety of biomaterials, including polymers, hydroxyapatite, and metals, thus improving the biocompatibility of the biomaterials. (Jones et al., U.S. Patent No. 5,585,267; El Ghannam et al., J. Biomed. Mater. Res. 1998 Jul; 41(1):30-40)

Thus, in a further aspect, the present invention comprises medical devices with improved biocompatibility, wherein the devices are coated with the r-laminin 5 of the invention, alone or in combination with other proteins or agents that serve to increase the biocompatibility of the device surface. The coated device stimulates cell attachment and provides for diminished inflammation and/or infection at the site of entry of the appliance. The device may also be used to stimulate gum junctional epithelium adhesion in the treatment of gingivitis and periodontitis.

Preferably, the device is a shaped article that is either an indwelling or transcutaneous catheter, polytetrafluoroethylene (PTFE), expanded PTFE (EPTFE), needle, metal pin, metal rod, colostomy tube, transcutaneous catheter, dental abutment piece or surgical mesh. In another aspect of this preferred embodiment, the device is used in vivo. Preferably, the appliance is made of or coated with a biocompatible metal that may be either stainless steel or titanium. Alternatively, the device is made of or coated with a ceramic material, or a polymer including but not limited to polyester, polyglycolic acid or a polygalactose-polyglycolic acid copolymer.

One particular use of the present invention is to increase epithelial cell adhesion to target surfaces. For example, prostheses for dental implantation may be coated with the r-laminin 5 of the invention to stimulate periodontal cell attachment. These prostheses typically comprise two separate pieces, an implant which is inserted into the bone and an abutment piece which actually contacts the junctional epithelium. Alternatively, the implant and abutment piece may be obtained as a single unit.

If the device is made of a natural or synthetic biodegradable material in the form of a mesh, sheet or fabric, the r-laminin 5 may be applied directly to the surface thereof. Epithelial cells may then be cultured on the matrix to form transplantable or implantable devices, including dental abutment pieces, needles, metal pins or rods, indwelling catheters, colostomy tubes, surgical meshes and any other appliance for which coating with the r-laminin is desirable. Alternatively, the devices may be implanted and cells may be permitted to attach in vivo. The epithelial cell-coated surgical meshes will be useful for skin allografts necessitated by compromised skin integrity.

Coupling of the r-laminin 5 may be non-covalent (such as by adsorption), or by covalent means. The device may be immersed in, incubated in, or sprayed with the r-laminin 5 of the invention. In a preferred embodiment, the concentration of r-laminin 5 for coating the device is between about 1 ng/ml and about 10 mg/ml.

The present invention also provides a method for inducing epithelial cell attachment to the device (as disclosed above), comprising coating the appliance with r-laminin 5 prior to incubation with epithelial cells.

The therapeutic application of r-laminin 5 produced in accordance with the present invention can be used for the treatment of a variety of conditions and diseases, including but not limited to Type I diabetes; skin conditions including but not limited to diabetic foot ulcers, venous ulcers, pressure sores, skin surgery, burns, acute wounds, and skin grafts; corneal ulcerations; gastro-intestinal ulcers; periodontitis; and gingivitis. The therapeutically effective amount of r-laminin 5 for use in these conditions and diseases can be readily ascertained by one of ordinary skill in the art.

The present invention may be better understood with reference to the accompanying examples that are intended for purposes of illustration only and should not be construed to limit the scope of the invention, as defined by the claims appended hereto.

Examples

Production of r-laminin-5 involved sequential transfections of a mammalian cell line with vectors containing cDNAs that encode for the chains of the laminin-5 molecule, namely α3, β3 and γ2. An additional polynucleotide sequence that encodes the 'flag' peptide (DYKDDDDK), was added to the amino terminus end of the β3 gene to facilitate affinity purification of the expressed heterotrimeric recombinant laminin-5 molecule.

IV. Materials and Methods

Expression vector constructs for α3

The entire coding sequence of the α3 cDNA [SEQ ID NO:1] was cloned via standard techniques into the expression vector pcDNA3.1/Zeo (Invitrogen), which contains the Zeocin resistant gene for selection. The expression vectors were used to produce stable cell lines according to the manufacturer's instructions.

In order to produce a second α3 expression vector, the full-length α3 cDNA was excised from the pZeoα3 expression construct by digestion with KpnI-NotI restriction enzymes. The double digested α3 fragment was inserted in the expression vector pTargeT (Promega; Madison, WI), generating pTgTα3. This expression construct carries the G418 resistant gene for selection of resistant clones. Both expression constructs have been analyzed by restriction enzyme mapping and DNA sequencing.

Construction of full-length β3 chain

Two cDNA fragments, Kal5-5c and Kal92-1, each cloned into separate pCR II vectors (Invitrogen), which together encode the entire β3 chain of laminin-5 [**SEQ ID NO:19**], were received from Dr. Burgeson's laboratory (4). The two fragments were cloned into a single vector to obtain the full-length β3 chain, plasmid PCRIIβ3.

Expression vector constructs for β3

The laminin β3 expression vector, pRCX3$\beta3_F$, was constructed containing the full-length β3 chain obtained for pCRIIβ3 and the FLAG epitope added to the amino terminus [**SEQ ID NO:17-18**]. pRCX3 is a vector derived from pRC/CMV (Invitrogen) and it contains a Geneticin resistant gene for selection with G418 sulfate, a BM 40 (SPARC) signal peptide sequence and the Flag peptide sequence in frame with convenient cloning sites

A second β3 expression vector was constructed by excising the complete laminin β3-flag peptide coding region from pRCX3$\beta3_F$ plasmid and introducing it into pcDNA3.1/Zeo. This expression constructs carries the Zeocin resistant gene for selection.

Both β3-expression constructs have been analyzed by restriction enzyme mapping and DNA sequencing.

Expression vector constructs for γ2

The full-length γ2 cDNA [**SEQ ID NO:29**] was excised from pVL1393γ2 (received from Dr. Karl Tryggvason, Karolinska Institute, Sweden) by digestion with BamH I-Xba I restriction enzymes. The double digested γ2 fragment was inserted in the corresponding sites of the expression vector pcDNA3.1/Zeo (Invitrogen), generating the pZeoγ2 expression construct. This expression constructs carries the Zeocin resistant gene for selection.

Similarly, a BamH I-Not I full-length γ2 cDNA fragment was cloned into the expression vector pTargeT (Promega), generating pTgTγ2. This expression construct carries the G418 resistant gene for selection of resistant clones.

Both expression constructs have been analyzed by restriction enzyme mapping and DNA sequencing.

Sequence analysis of expression constructs

The expression vector constructs have been sequenced and the reported gene sequences compared to the published sequences. **Table 2** shows a summary of the amino acid mismatches for the different laminin chains.

α3 chain: the reported sequence matched the published sequence.

β3 chain: several discrepancies with the published sequence were found. Single and multiple base deletions and insertions are present along the sequence. These base changes generated some silent mutations, amino acid substitutions and insertion of amino acids. These changes do not cause early termination codons. Therefore, the β3 chain seems to be of "full-length" and the protein is being produced.

γ2 chain: This chain was reported to have 3 base changes creating 3 amino acid substitutions.

Table 2: Summary of amino acid differences from those reported in the literature

Laminin chain	Amino acid change
α3	None
β3	P, insertion at position 251-2
	A_{372} --P_{372}
	$R_{408}R_{409}$--$Q_{408}G_{409}$
	R, insertion at position 421
	P_{584}—R_{584}
	A_{796}—G_{796}
	$R_{894}S_{895}E_{896}$--$S_{894}E_{895}A_{896}$
γ2	R_{168}—G_{168}
	I_{473}—M_{473}
	S_{521}—N_{521}

Transfection of human kidney 293 cells

Wild type human kidney 293 cells were transfected with the different expression constructs utilizing standard techniques. Two transfection reagents were used, LIPOFECTAMINE™ from GIBCO (Rockville, MD) and SUPERFECT™ from Qiagen (Valencia, CA). Experiments (see below) suggested that the 293 cells do not express detectable endogenous laminin α3, β3, or γ2 chains

Briefly, both methods required mixing the transfection reagent with the DNA of interest, incubating for a brief period at room temperature, and adding the mixture to the cells. The cells were split the previous day so they were at 50-80% confluency the day of the transfection. The incubation with the DNA-reagent complexes was conducted for 2-3 hours in serum free media for LIPOFECTAMINE™ transfection or complete media for SUPERFECT™ transfection. After this incubation period the media was replaced with fresh growth media and the incubation was continued until the selection process begins.

The selection process was carried out in DMEM F12/10% FBS containing either Geneticin (G418 sulfate) at 400 μg/ml for selection of G418 resistants, or Zeocin at 50 μg/ml for selection of Zeocin resistants. After splitting to selective media, the cells were fed every two days with fresh selective media, until cell foci were identified. Clones transfected with the three laminin chains and secreting r-laminin 5 into the medium were selected with media containing both antibiotics.

Results

Media from human kidney 293 cells transfected with a single laminin chain were initially analyzed on Western blots using chain-specific anti-laminin-5 antibodies. Cell fractions, as well as "whole" fractions containing cells plus any deposited "matrix-like" material obtained by scraping the cells into loading buffer, were also analyzed. Western blot analysis of wild type 293 cell cultures showed no detectable laminin α3, β3, or γ2 chain proteins.

The expression of single laminin chains following transfection is generally intracellular, except for a few β3 clones that appear to show β3 chain reactivity in the media in Western blot analyses using the anti-FLAG antibody.

All clones showing FLAG antibody reactivity were verified by PCR to confirm the incorporation of the transfected gene. Analysis of genomic DNA preparations from such clones by PCR was done using laminin chain-specific primer pairs. The amplified products were compared to positive controls where the original expression constructs were used as templates. Results are shown in **Table 3**. A few selected clones were analyzed by RT-PCR using the same laminin chain-specific primers and total RNA and/or mRNA preparations as templates. These results are also shown in **Table 2**.

Other data (not shown) demonstrated that the molecular sizes of some of the components of r-laminin 5 were different from those in purified laminin 5. Particularly, the major component of the α3 chain in purified laminin 5 was 165 kD, while the α3 band in r-laminin 5 migrated as two chains of 150 kD and 95 kD.

Identified co-transfected clones producing all three chains (as assessed by both genomic PCR and RT-PCR analysis), were further analyzed in a keratinocyte cell adhesion binding assay.

HFK cell adhesion assay for laminin-5. The method used measures laminin-5 activity present in conditioned media from various clones. Any laminin-5 present in the test media was trapped to a 96 well via an anti-laminin α3 antibody (C 25). Human foreskin keratinocytes (HFK) were labeled fluorescently, added to the treated wells, and allowed to adhere for 30 minutes. Fluorescence was measured before and after washing with PBS. The % cell adhesion is equal to fraction of fluorescence retained in the well. As controls, cells were pre-incubated with an anti-integrin α3β1 inhibitory antibody (P1B5)(α3β1 is the cell receptor for laminin 5), or non-specific control antibody (SP2)

before being added to the wells. Media controls (Keratinocyte growth media ("KGM"); or DMEM F12 culture media ("medium") were also used. The "$a2_F$" notation denotes culture medium from 293 cells transfected to express an unrelated FLAG-containing protein.

The results, shown in **Table 2** (last column) and in **Figure 1**. The figure is labeled as follows: C5 and F10: conditioned culture media from r-laminin-5 producing clones C5 and F10; *C6 and *F10: conditioned culture media collected earlier and kept refrigerated. These data demonstrated that media from several clones produced positive results in the cell adhesion assay, indicating the r-laminin-5 produced by these clones is biologically active. The activity was inhibited in the presence of an integrin $\alpha 3\beta 1$ antibody, demonstrating that the r-laminin 5 is binding to the cells via the $\alpha 3\beta 1$ integrin.

To assist in the purification of the heterotrimer r-laminin-5 molecule, the laminin $\beta 3$ chain was labeled with a 'flag' sequence at the amino terminus end. Media from clones transfected with all three chains, and shown to express all three chains, were passed through an anti-flag column and eluted with excess flag peptide. The eluted fractions were analyzed by gel electrophoresis. The data demonstrate that r-laminin 5 was produced and isolated.

Table 3: Summary analysis of selected r-L5 clones

Clone	Western Blot				PCR[1]			RT-PCR[2]			Adhesion
	α3	β3	γ2	Flag	α3	β3	γ2	α3	β3	γ2	Assay
A2-3	-	nd	nd	+	-	+	+	-	+	+	-
A4-3	+	+	+	+	+	+	+	+	+	+	+
A10-3	-	nd	+	+	-	+	-	-	+	+	-
B1-6	nd	nd	nd	+	+	+	+	+	+	+	+
C2-3	-	nd	+	+	-	+	+	+	+	+	-
C5-7	nd	nd	nd	+	+	+	+	nd	+	+	-
C6-3	+	+	+	+	+	+	+	+	+	+	+
C10-3	-	nd	nd	+	-	+	+	+	+	+	-
E1-3	-	nd	nd	-	-	+	-	-	+	+	-
E2-3	-	nd	+	+	-	+	-	+	+	+	-
E7-3	-	nd	-	+	-	+	-	-	+	+	-
F10-5	nd	nd	nd	+	+	+	+	+	+	+	+

nd = Not determined

1. PCR analysis of genomic DNA preparations were performed using laminin chain-specific primer pairs. The amplified products were compared to positive controls where the original expression constructs were used as templates.
2. RT-PCR analyses were done similarly using total RNA and/or mRNA as templates and primers as above.

Several of the above clones were selected for further analysis. A 1 liter culture from clone F10-5 was prepared, and r-laminin 5 was purified using the methods described above. The r-laminin 5 was used in an HFK cell adhesion assay exactly as described above, except that r-laminin 5 was coated directly onto the plate. The results are presented in **Figure 2** and demonstrate that r-laminin 5 markedly increases adhesion of HFK cells at all concentrations tested.

Electron Micrograph Analysis

Purified r-laminin 5 protein was diluted to 50 μg/ml and adjusted to 70% glycerol/30% 0.15M ammonium bicarbonate and rotary shadowed using standard techniques. **Figure 3** shows an 80,000X magnification field of (A) r-laminin 5; and (B) "native" laminin 5 (purified by BM165 monoclonal antibody affinity chromatography from SCC-25 (squamous cell carcinoma cell line) conditioned medium). The bar represents 50 nm. These results demonstrated that both the r-laminin 5 and the "native" purified laminin 5 formed similar cross-shaped structures typical of laminins.

The present invention is not limited by the aforementioned particular preferred embodiments. It will occur to those ordinarily skilled in the art that various modifications may be made to the disclosed preferred embodiments without diverting from the concept of the invention. All such modifications are intended to be within the scope of the present invention.

We claim

1. Recombinant laminin 5-expressing cells.

2. The recombinant laminin 5-expressing cells of claim 1, wherein the cells express recombinant laminin 5 comprising:

a first chain comprising a polypeptide that is substantially similar to an α3 laminin chain;

a second chain comprising a polypeptide that is substantially similar to a β3 laminin chain; and

a third chain comprising a polypeptide that is substantially similar to a γ2 laminin chain;

wherein the first, second, and third chains are assembled into recombinant heterotrimeric laminin 5.

3. The recombinant laminin 5-expressing cells of claim 1, wherein the cells express recombinant laminin 5 comprising:

a first chain comprising a recombinant polypeptide that is at least 70% identical to one or more of SEQ ID NO:2, 4, 6, 8, 10,12, or fragments thereof;

a second chain comprising a recombinant polypeptide that is at least 70% identical to one or more of SEQ ID NO:14, 16, 18, 20, 22, 24, or fragments thereof; and

a third chain comprising a recombinant polypeptide that is at least 70% identical to one or more of SEQ ID NO:26, 28, 30, 32, 34, 36, or fragments thereof;

wherein the cell expresses the first, second, and third chains, and wherein the first, second, and third chains assemble into recombinant heterotrimeric laminin 5 that is secreted into the media by the cultured cell.

4. The recombinant laminin 5-expressing cells of claim 1, wherein the cells express recombinant laminin 5 comprising:

a first chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO:1, 3, 5, 7, 9, 11, or fragments thereof;

a second chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO:13, 15, 17, 19, 21, 23, or fragments thereof; and

a third chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO: 25, 27, 29, 31, 33, 35, or fragments thereof;

wherein the cell expresses the first, second, and third chains, and wherein the first, second, and third chains assemble into recombinant heterotrimeric laminin 5 that is secreted into the media by the cultured cell.

5. The recombinant laminin 5-expressing host cells of claim 1, wherein the cells express recombinant laminin 5 comprising a first, second, and third polypeptide chain, wherein the first, second, and third polypeptide chains each comprise a general structure selected from the group consisting of: (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e)

wherein R1 is a amino terminal methionine; R2 is a signal sequence that is capable of directing secretion of the polypeptide, wherein the signal sequence may be the natural signal sequence for the particular laminin chain, that of another secreted protein, or it may be an artificial sequence; R3 is a secreted $\alpha 3$ laminin chain for the first polypeptide chain, a secreted $\beta 3$ laminin chain for the second polypeptide chain, and $\gamma 2$ laminin chain for the third polypeptide chain; and R3(e) is identical to R3, but further comprises an epitope tag .

6. A method of purifying recombinant laminin 5, comprising:

a. providing the eukaryotic cells of any one of claim 1-5;

b. growing the cells in cell culture medium under conditions to stimulate expression of the recombinant laminin 5 chains;

c. passing the cell culture medium through an affinity chromatography column, wherein the column contains a compound that specifically binds to the epitope tag;

d. washing the affinity column to remove unbound materials; and

e. eluting the bound recombinant laminin 5 from the column.

7. Purified recombinant laminin 5 isolated according to the method of claim 6.

8. Purified recombinant laminin 5.

9. The substantially purified recombinant laminin 5 of claim 8 comprising:

a first chain comprising a polypeptide that is substantially similar to an α3 laminin chain;

a second chain comprising a polypeptide that is substantially similar to a β3 laminin chain; and

a third chain comprising a polypeptide that is substantially similar to a γ2 laminin chain;

wherein the first, second, and third chains are assembled into recombinant heterotrimeric laminin 5.

10. The purified recombinant laminin 5 of claim 8, comprising:

a first chain comprising a recombinant polypeptide that is at least 70% identical to one or more of SEQ ID NO:2, 4, 6, 8, 10, 12, or fragments thereof;

a second chain comprising a recombinant polypeptide that is at least 70% identical to one or more of SEQ ID NO:14, 16, 18, 20, 22, 24, or fragments thereof; and

a third chain comprising a recombinant polypeptide that is at least 70% identical to one or more of SEQ ID NO:26, 28, 30, 32, 34, 36, or fragments thereof;

wherein the first, second, and third chains are assembled into recombinant heterotrimeric laminin 5.

11. The purified recombinant laminin 5 of claim 8, comprising:

a first chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO:1, 3, 5, 7, 9, 11, or fragments thereof;

a second chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO:13, 15, 17, 19, 21, 23, or fragments thereof; and

a third chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of SEQ ID NO: 25, 27, 29, 31, 33, 35, or fragments thereof;

wherein the first, second, and third chains are assembled into recombinant heterotrimeric laminin 5.

12. The purified recombinant heterotrimeric laminin 5 of claim 8, comprising a first, second, and third polypeptide chain, wherein the first, second, and third polypeptide chains each comprise a general structure selected from the group consisting of: (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e)

wherein R1 is a amino terminal methionine; R2 is a signal sequence that is capable of directing secretion of the polypeptide, wherein the signal sequence may be the natural signal sequence for the particular laminin chain, that of another secreted protein, or it may be an artificial sequence; R3 is a secreted α3 laminin chain for the first polypeptide chain, a secreted β3 laminin chain for the second polypeptide chain, and a secreted γ2 laminin chain for the third polypeptide chain; and R3(e) is identical to R3, but further comprises an epitope tag.

13. A pharmaceutical composition comprising:

a. the recombinant laminin 5 of any of claims 7-12; and

b. a pharmaceutically acceptable carrier.

14. A method for accelerating wound healing comprising administering to a patient in need thereof an amount effective of the recombinant laminin 5 of any of claims 7-12 to accelerate wound healing.

15. The method of claim 14 wherein the wound is selected from the group consisting of diabetic foot ulcers, venous ulcers, pressure sores, skin surgery, burns, acute wounds, skin grafts, corneal ulcerations, gastro-intestinal ulcers, periodontitis, and gingivitis.

16. A method to improve the biocompatibility of a medical device, comprising contacting the medical device with an amount effective of the recombinant laminin 5 of any of claims 7-12 to improve the biocompatibility of the medical device.

17. A method to promote cell adhesion to a surface, comprising contacting the cells with an amount effective of the recombinant laminin 5 of any of claims 7-12 to promote cell adhesion to a surface.

18. An improved method for the ex vivo treatment of Type I diabetes in a patient in need thereof, wherein the improvement consists of culturing isolated pancreatic islet beta in the presence of an amount effective the recombinant laminin 5 of any of claims 7-12 to promote adhesion of the pancreatic islet beta cells to a surface, culturing the cells, and re-introducing the cells into the patient.

19. A method for regulating angiogenesis, comprising contacting a tissue in need thereof with an amount effective to promote angiogenesis of laminin 5 to regulate angiogenesis.

20. The method of claim 19, wherein the laminin 5 comprises recombinant laminin 5 according to any one of claims 7-12.

21. An improved cell growth substrate, wherein the improvement consists of providing a cell growth substrate that has been coated with an amount effective of the recombinant laminin 5 of any of claims 7-12 to promote cell attachment to the cell growth substrate.

22. An improved cell culture medium, wherein the improvement consists of providing an amount effective of the recombinant laminin 5 of any of claims 7-12 to promote cell attachment to a cell growth substrate.

23. An improved medical implantation device, wherein the improvement consists of providing a medical implantation device that has been coated with an amount effective of the recombinant laminin 5 of any of claims 7-12 to promote cell attachment to the medical implantation device.

24. The improved medical implantation device of claim 23, wherein the medical implantation device is selected from the group consisting of artificial grafts, indwelling or transcutaneous catheter, polytetrafluoroethylene, expanded polytetrafluoroethylene, needle, metal pin, metal rod, colostomy tube, transcutaneous catheter, dental abutment piece or surgical mesh.

25. A method for accelerating wound healing comprising administering to a patient in need thereof an amount effective of the pharmaceutical composition of claim 13 to accelerate wound healing.

26. The method of claim 25 wherein the wound is selected from the group consisting of diabetic foot ulcers, venous ulcers, pressure sores, skin surgery, burns, acute wounds, skin grafts, corneal ulcerations, gastro-intestinal ulcers, periodontitis, and gingivitis.

27. A method to improve the biocompatibility of a medical device, comprising contacting the medical device with an amount effective of the pharmaceutical composition of claim 13 to improve the biocompatibility of the medical device.

28. A method to promote cell adhesion to a surface, comprising contacting the cells with an amount effective of the pharmaceutical composition of claim 13 to promote cell adhesion to a surface.

29. An improved method for the ex vivo treatment of Type I diabetes in a patient in need thereof, wherein the improvement consists of culturing isolated pancreatic islet beta in the presence of an amount effective the pharmaceutical composition of claim 13 to promote adhesion of the pancreatic islet beta cells to a surface, culturing the cells, and re-introducing the cells into the patient.

30. A method for regulating angiogenesis, comprising contacting a tissue in need thereof with an amount effective to regulate angiogenesis of the pharmaceutical composition of claim 13 to regulate angiogenesis.

31. An improved cell growth substrate, wherein the improvement consists of providing a cell growth substrate that has been coated with an amount effective of the pharmaceutical composition of claim 13 to promote cell attachment to the cell growth substrate.

32. An improved medical implantation device, wherein the improvement consists of providing a medical implantation device that has been coated with an amount effective of the pharmaceutical composition of claim 13 to promote cell attachment to the medical implantation device.

33. The improved medical implantation device of claim 32, wherein the medical implantation device is selected from the group consisting of artificial grafts, indwelling or transcutaneous catheter, polytetrafluoroethylene, expanded polytetrafluoroethylene, needle, metal pin, metal rod, colostomy tube, transcutaneous catheter, dental abutment piece or surgical mesh.

34. An isolated polynucleotide sequence selected from the group consisting of SEQ ID 21, SEQ ID NO:23, SEQ ID NO:29, SEQ ID NO:31.

35. An isolated polypeptide sequence selected from the group consisting of SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:30, and SEQ ID NO:32.

FIG. 1

Figure 1 : HFK cell adhesion assay

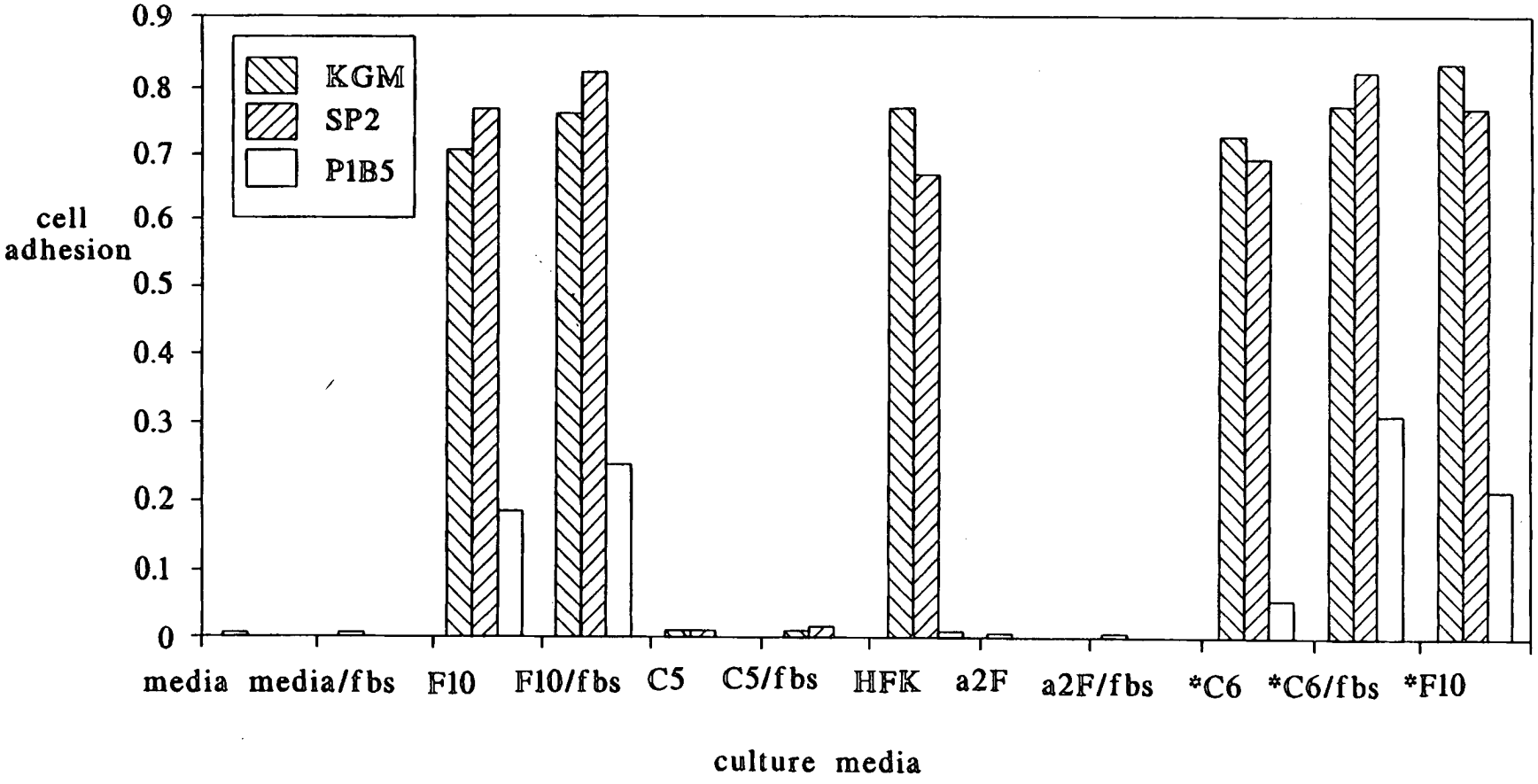


FIG. 2

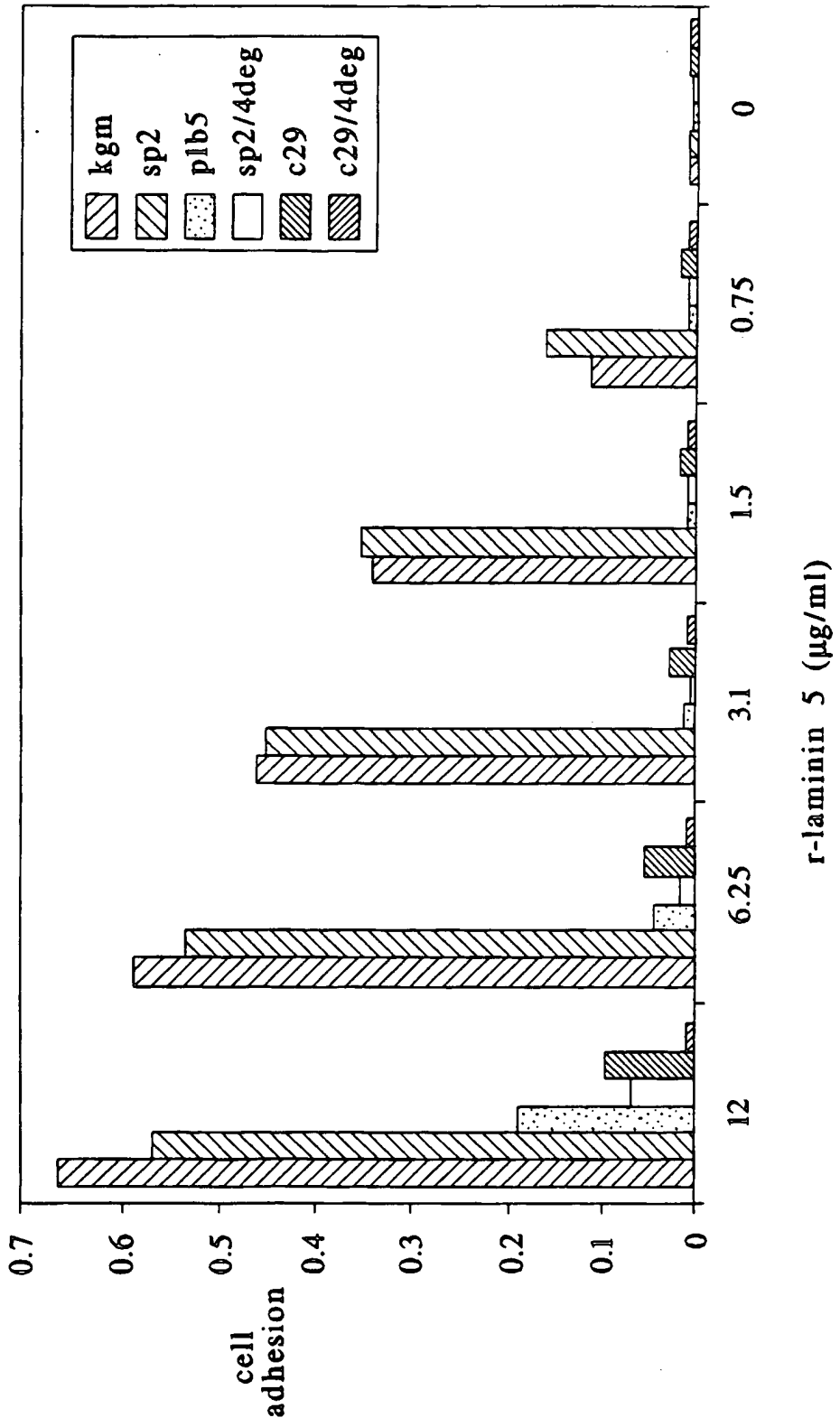
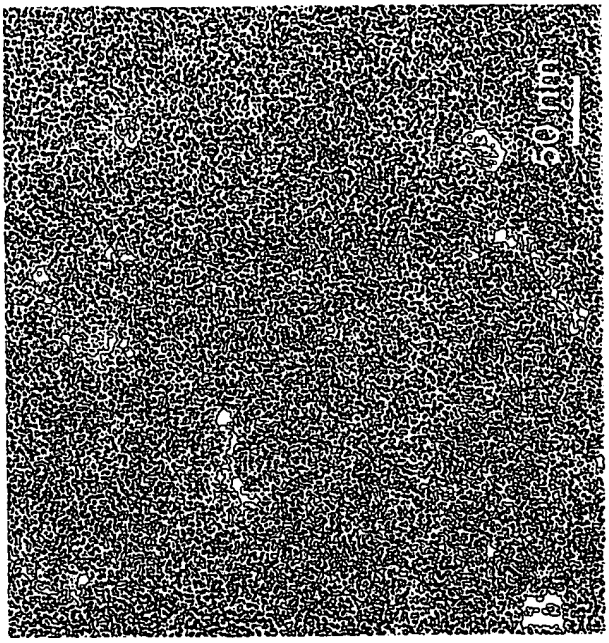
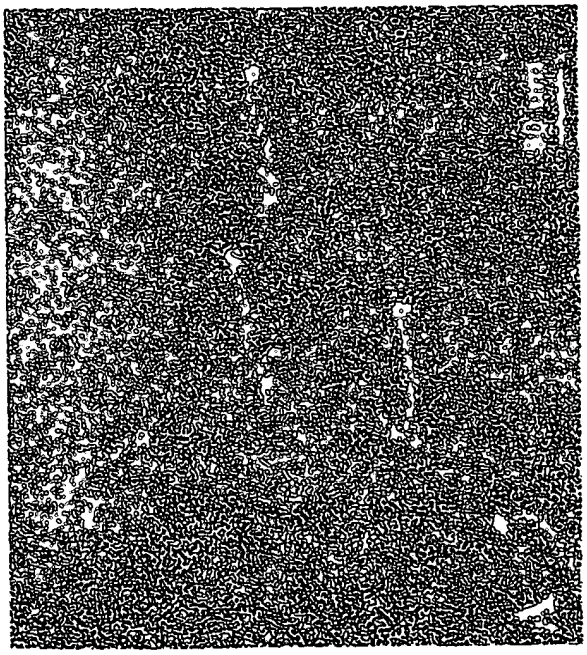

HFK adhesion to purified r-laminin 5
kgm
sp2
plb5
sp2/4deg
c29
c29/4deg
cell adhesion
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
12
6.25
3.1
1.5
0.75
0
r-laminin 5 (µg/ml)

Figure 3

Rotary-shadowed electron micrographs of recombinant laminin 5 (A) and "native" laminin 5 (B).





SEQUENCE LISTING

<110> Boutand, Ariel

<120> Recombinant Laminin 5

<130> 99-274-C1

<140> To Be Assigned
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<160> 36

<170> PatentIn Ver. 2.0

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Tyr Ser Ser Gln Gln Gln Arg Val Pro Phe Leu Gln Pro Pro Gly Gln
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Ser Gln Leu Gln Ala Ser Tyr Val Glu Phe Arg Pro Ser Gln Gly Cys
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agc cct gga tac tat cgg gat cat aaa ggc ttg tat acc gga cgg tgt 242
Ser Pro Gly Tyr Tyr Arg Asp His Lys Gly Leu Tyr Thr Gly Arg Cys
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Val Pro Cys Asn Cys Asn Gly His Ser Asn Gln Cys Gln Asp Gly Ser
80 85 90

ggc ata tgt gtt aac tgt cag cac aac acc gcg gga gag cac tgt gaa 338
Gly Ile Cys Val Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu
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Arg Cys Gln Glu Gly Tyr Tyr Gly Asn Ala Val His Gly Ser Cys Arg
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aat ggg gga gac gtg cgg tgc tcc tgc aaa gct ggg tac aca gga aca   482
Asn Gly Gly Asp Val Arg Cys Ser Cys Lys Ala Gly Tyr Thr Gly Thr
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cag tgt gaa agg tgt gca ccg gga tat ttc ggg aat ccc cag aaa ttc   530
Gln Cys Glu Arg Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe
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gga ggt agc tgc caa cca tgc agt tgt aac agc aat ggc cag ctg ggc   578
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agc tgt cat ccc ctg act gga gac tgc ata aac caa gaa ccc aaa gat   626
Ser Cys His Pro Leu Thr Gly Asp Cys Ile Asn Gln Glu Pro Lys Asp
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agc agc cct gca gaa gaa tgt gat gat tgc gac agc tgt gtg atg acc   674
Ser Ser Pro Ala Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr
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Leu Leu Asn Asp Leu Ala Thr Met Gly Glu Gln Leu Arg Leu Val Lys
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Arg His Met Glu Thr Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Asn
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aga gaa ctg act gat ttg aat caa gaa ttt gag act tta caa gaa aag   914
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cgg gca aca caa agc gca aaa gaa cta gat gtg aag att aaa aat gtc   1010
Arg Ala Thr Gln Ser Ala Lys Glu Leu Asp Val Lys Ile Lys Asn Val
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380                 385                 390                 395

cgg ata agg acc tgg cag aaa acc cac cag ggg gag aac aat ggg ctt   1250
Arg Ile Arg Thr Trp Gln Lys Thr His Gln Gly Glu Asn Asn Gly Leu
                400                 405                 410

gct aac agt atc cgg gat tct tta aat gaa tac gaa gcc aaa ctc agt   1298
Ala Asn Ser Ile Arg Asp Ser Leu Asn Glu Tyr Glu Ala Lys Leu Ser
            415                 420                 425

gac ctt cgt gct cgg ctg cag gag gca gct gcc caa gcc aag cag gca   1346
Asp Leu Arg Ala Arg Leu Gln Glu Ala Ala Ala Gln Ala Lys Gln Ala
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acc act gca gac tca tct ttg ttg caa acc aac att gcg ctg cag ctg   1490
Thr Thr Ala Asp Ser Ser Leu Leu Gln Thr Asn Ile Ala Leu Gln Leu
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Met Glu Lys Ser Gln Lys Glu Tyr Glu Lys Leu Ala Ala Ser Leu Asn
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Ala Gly Lys Thr Ser Leu Val Glu Glu Ala Glu Lys His Ala Arg Ser
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tta caa gag ctg gca aag cag ctg gaa gag atc aag aga aac gcc agc   1682
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ggg gat gag ctg gtg cgc tgt gct gtg gat gcc gcc acc gcc tac gag   1730
Gly Asp Glu Leu Val Arg Cys Ala Val Asp Ala Ala Thr Ala Tyr Glu
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aac atc ctc aat gcc atc aaa gcg gcc gag gac gca gcc aac agg gct   1778
Asn Ile Leu Asn Ala Ile Lys Ala Ala Glu Asp Ala Ala Asn Arg Ala
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620                 625                 630                 635

ctc aac aac cta cag caa acc ctg aat att gtg aca gtt cag aaa gaa   1970
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gtg ata gac acc aat ctc aca act ctc cga gat ggt ctt cat ggg ata   2018
Val Ile Asp Thr Asn Leu Thr Thr Leu Arg Asp Gly Leu His Gly Ile
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cag aga ggt gat att gat gct atg atc agt agt gca aag agc atg gtc   2066
Gln Arg Gly Asp Ile Asp Ala Met Ile Ser Ser Ala Lys Ser Met Val
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aga aag gcc aac gac atc aca gat gag gtt ctg gat ggg ctc aac ccc   2114
Arg Lys Ala Asn Asp Ile Thr Asp Glu Val Leu Asp Gly Leu Asn Pro
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Ile Gln Thr Asp Val Glu Arg Ile Lys Asp Thr Tyr Gly Arg Thr Gln
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Lys Leu Thr Asn Lys Leu Pro Asp Leu Trp Arg Lys Ile Glu Ser Ile
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aac caa cag ctg ttg ccc ttg gga aac atc tct gac aac atg gac aga   2306
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gtc ccc atg agg ttc aat ggt aaa tct gga gtc gaa gtc cga ctg cca   2402
Val Pro Met Arg Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro
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caa agg ccc aac tca aga gaa aat ggg ggt act gag aat atg ttt gtg   2498
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atg tac ctt gga aat aaa gat gcc tcc cgg gac tac atc ggc atg gca   2546
Met Tyr Leu Gly Asn Lys Asp Ala Ser Arg Asp Tyr Ile Gly Met Ala
        830                 835                 840

gtt gtg gat ggc cag ctc acc tgt gtc tac aac ctg ggg gac cgt gag   2594
Val Val Asp Gly Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu
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gca gtt atg gat cgg gtg aaa ttt cag aga att tat cag ttt gca agg   2690
Ala Val Met Asp Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Arg
                880                 885                 890

ctt aat tac acc aaa gga gcc aca tcc agt aaa cca gaa aca ccc gga   2738
Leu Asn Tyr Thr Lys Gly Ala Thr Ser Ser Lys Pro Glu Thr Pro Gly
            895                 900                 905

gtc tat gac atg gat ggt aga aat agc aat aca ctc ctt aat ttg gat   2786
Val Tyr Asp Met Asp Gly Arg Asn Ser Asn Thr Leu Leu Asn Leu Asp
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cct gaa aat gtt gta ttt tat gtt gga ggt tac cca cct gat ttt aaa   2834
Pro Glu Asn Val Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Lys
    925                 930                 935

ctt ccc agt cga cta agt ttc cct cca tac aaa ggt tgt att gaa tta   2882
Leu Pro Ser Arg Leu Ser Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu
940                 945                 950                 955

gat gac ctc aat gaa aat gtt ctg agc ttg tac aac ttc aaa aaa aca   2930
Asp Asp Leu Asn Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Lys Thr
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ttc aat ctc aac aca act gaa gtg gag cct tgt aga agg agg aag gaa   2978
Phe Asn Leu Asn Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu
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gag tca gac aaa aat tat ttt gaa ggt acg ggc tat gct cga gtt cca   3026
Glu Ser Asp Lys Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Val Pro
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act caa cca cat gct ccc atc cca acc ttt gga cag aca att cag acc   3074
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acc gtg gat aga ggc ttg ctg ttc ttt gca gaa aac ggg gat cgc ttc   3122
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aat tca gag cta cca aaa gag aga gga gtt gga gac gcc ata aac aac   3218
Asn Ser Glu Leu Pro Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn
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ggc aga gac cat tcg att cag atc aaa att gga aaa ctc caa aag cgt   3266
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acc aaa aag tgc tcg gaa gac tgg aag ctt gtg cga tct gcc tca ttc   3506
Thr Lys Lys Cys Ser Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe
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tcc aga gga gga caa ttg agt ttc act gat ttg ggc tta cca cct act   3554
Ser Arg Gly Gly Gln Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr
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gac cac ctc cag gcc tca ttt gga ttt cag acc ttt caa ccc agt ggc   3602
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gaa gat ggt tac att gaa ttg agc acc agc gat agc ggc ggc cca att   3698
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          1215                1220                1225

ttt aaa tct cca cag acg tat atg gat ggt tta ctg cat tat gta tct   3746
Phe Lys Ser Pro Gln Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser
       1230                1235                1240

gta ata agc gac aac tct gga cta cgg ctt ctc atc gat gac cag ctt   3794
Val Ile Ser Asp Asn Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu
   1245                1250                1255

ctg aga aat agc aaa agg cta aaa cac att tca agt tcc cgg cag tct   3842
Leu Arg Asn Ser Lys Arg Leu Lys His Ile Ser Ser Ser Arg Gln Ser
1260              1265                1270                1275

ctg cgt ctg ggc ggg agc aat ttt gag ggt tgt att agc aat gtt ttt   3890
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gtc cag agg tta tca ctg agt cct gaa gtc cta gat ttg acc agt aac   3938
Val Gln Arg Leu Ser Leu Ser Pro Glu Val Leu Asp Leu Thr Ser Asn
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tct ctc aag aga gat gtg tcc ctg gga ggc tgc agt tta aac aaa cca   3986
Ser Leu Lys Arg Asp Val Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro
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cct ttt cta atg ttg ctt aaa ggt tct acc agg ttt aac aag acc aag   4034
Pro Phe Leu Met Leu Leu Lys Gly Ser Thr Arg Ph  Asn Lys Thr Lys
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Arg Ser Val Lys Val Trp Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr
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Gln Ala Asn His Gly Ala Leu Gln Phe Gly Asp Ile Pro Thr Ser His
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ttg cta ttc aag ctt cct cag gag ctg ctg aaa ccc agg tca cag ttt   4226
Leu Leu Phe Lys Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe
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gct gtg gac atg cag aca aca tcc tcc aga gga ctg gtg ttt cac acg   4274
Ala Val Asp Met Gln Thr Thr Ser Ser Arg Gly Leu Val Phe His Thr
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Gly Thr Lys Asn Ser Phe Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu
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Val Phe Ala Leu Gly Thr Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys
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gag aaa tgc aat gat ggg aaa tgg cac acg gtg gtg ttt ggc cat gat   4418
Glu Lys Cys Asn Asp Gly Lys Trp His Thr Val Val Phe Gly His Asp
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ggg gaa aag ggg cgc ttg gtt gtg gat gga ctg agg gcc cgg gag gga   4466
Gly Glu Lys Gly Arg Leu Val Val Asp Gly Leu Arg Ala Arg Glu Gly
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agt ttg cct gga aac tcc acc atc agc atc aga gcg cca gtt tac ctg   4514
Ser Leu Pro Gly Asn Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu
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gga tca cct cca tca ggg aaa cca aag agc ctc ccc aca aac agc ttt   4562
Gly Ser Pro Pro Ser Gly Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe
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Val Gly Cys Leu Lys Asn Phe Gln Leu Asp Ser Lys Pro Leu Tyr Thr
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cct tct tca agc ttc ggg gtg tct tcc tgc ttg ggt ggt cct ttg gag   4658
Pro Ser Ser Ser Phe Gly Val Ser Ser Cys Leu Gly Gly Pro Leu Glu
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Lys Gly Ile Tyr Phe Ser Glu Glu Gly Gly His Val Val Leu Ala His
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Ser Val Leu Leu Gly Pro Glu Phe Lys Leu Val Phe Ser Ile Arg Pro
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                1600                1605                1610

agt ggg gca ggt ggg acc tca acg tcg gtc aca cca aag cag tct ctg   4898
Ser Gly Ala Gly Gly Thr Ser Thr Ser Val Thr Pro Lys Gln Ser Leu
            1615                1620                1625

tgt gat gga cag tgg cac tcg gtg gca gtc acc ata aaa caa cac atc   4946
Cys Asp Gly Gln Trp His Ser Val Ala Val Thr Ile Lys Gln His Ile
        1630                1635                1640

ctg cac ctg gaa ctg gac aca gac agt agc tac aca gct gga cag atc   4994
Leu His Leu Glu Leu Asp Thr Asp Ser Ser Tyr Thr Ala Gly Gln Ile
    1645                1650                1655

ccc ttc cca cct gcc agc act caa gag cca cta cac ctt gga ggt gct   5042
Pro Phe Pro Pro Ala Ser Thr Gln Glu Pro Leu His Leu Gly Gly Ala
1660                1665                1670                1675

cca gcc aat ttg acg aca ctg agg atc cct gtg tgg aaa tca ttc ttt   5090
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                1680                1685                1690

ggc tgt ctg agg aat att cat gtc aat cac atc cct gtc cct gtc act   5138
Gly Cys Leu Arg Asn Ile His Val Asn His Ile Pro Val Pro Val Thr
            1695                1700                1705

gaa gcc ttg gaa gtc cag ggg cct gtc agt ctg aat ggt tgt cct gac   5186
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        1710                1715                1720

cag taacccaagc ctatttcaca gcaaggaaat tcaccttcaa aagcactgat        5239
Gln

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             20                  25                  30

Gln Arg Val Pro Phe Leu Gln Pro Pro Gly Gln Ser Gln Leu Gln Ala
         35                  40                  45

Ser Tyr Val Glu Phe Arg Pro Ser Gln Gly Cys Ser Pro Gly Tyr Tyr
     50                  55                  60

Arg Asp His Lys Gly Leu Tyr Thr Gly Arg Cys Val Pro Cys Asn Cys
 65                  70                  75                  80
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Asn Gly His Ser Asn Gln Cys Gln Asp Gly Ser Gly Ile Cys Val Asn
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Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Gln Glu Gly
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Tyr Tyr Gly Asn Ala Val His Gly Ser Cys Arg Ala Cys Pro Cys Pro
        115                 120                 125

His Thr Asn Ser Phe Ala Thr Gly Cys Val Val Asn Gly Gly Asp Val
    130                 135                 140

Arg Cys Ser Cys Lys Ala Gly Tyr Thr Gly Thr Gln Cys Glu Arg Cys
145                 150                 155                 160

Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys Gln
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Pro Cys Ser Cys Asn Ser Asn Gly Gln Leu Gly Ser Cys His Pro Leu
            180                 185                 190

Thr Gly Asp Cys Ile Asn Gln Glu Pro Lys Asp Ser Ser Pro Ala Glu
        195                 200                 205

Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp Leu
    210                 215                 220

Ala Thr Met Gly Glu Gln Leu Arg Leu Val Lys Ser Gln Leu Gln Gly
225                 230                 235                 240

Leu Ser Ala Ser Ala Gly Leu Leu Glu Gln Met Arg His Met Glu Thr
                245                 250                 255

Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Asn Tyr Arg Ser Ala Ile
            260                 265                 270

Ser Asn His Gly Ser Lys Ile Glu Gly Leu Glu Arg Glu Leu Thr Asp
        275                 280                 285

Leu Asn Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn Ser
    290                 295                 300

Arg Lys Ala Gln Thr Leu Asn Asn Asn Val Asn Arg Ala Thr Gln Ser
305                 310                 315                 320

Ala Lys Glu Leu Asp Val Lys Ile Lys Asn Val Ile Arg Asn Val His
                325                 330                 335

Ile Leu Leu Lys Gln Ile Ser Gly Thr Asp Gly Glu Gly Asn Asn Val
            340                 345                 350

Pro Ser Gly Asp Phe Ser Arg Glu Trp Ala Glu Ala Gln Arg Met Met
        355                 360                 365

Arg Glu Leu Arg Asn Arg Asn Phe Gly Lys His Leu Arg Glu Ala Glu
    370                 375                 380

Ala Asp Lys Arg Glu Ser Gln Leu Leu Leu Asn Arg Ile Arg Thr Trp
385                 390                 395                 400

Gln Lys Thr His Gln Gly Glu Asn Asn Gly Leu Ala Asn Ser Ile Arg
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                405                 410                 415

Asp Ser Leu Asn Glu Tyr Glu Ala Lys Leu Ser Asp Leu Arg Ala Arg
            420                 425                 430

Leu Gln Glu Ala Ala Ala Gln Ala Lys Gln Ala Asn Gly Leu Asn Gln
        435                 440                 445

Glu Asn Glu Arg Ala Leu Gly Ala Ile Gln Arg Gln Val Lys Glu Ile
    450                 455                 460

Asn Ser Leu Gln Ser Asp Phe Thr Lys Tyr Leu Thr Thr Ala Asp Ser
465                 470                 475                 480

Ser Leu Leu Gln Thr Asn Ile Ala Leu Gln Leu Met Glu Lys Ser Gln
                485                 490                 495

Lys Glu Tyr Glu Lys Leu Ala Ala Ser Leu Asn Glu Ala Arg Gln Glu
            500                 505                 510

Leu Ser Asp Lys Val Arg Glu Leu Ser Arg Ser Ala Gly Lys Thr Ser
        515                 520                 525

Leu Val Glu Glu Ala Glu Lys His Ala Arg Ser Leu Gln Glu Leu Ala
    530                 535                 540

Lys Gln Leu Glu Glu Ile Lys Arg Asn Ala Ser Gly Asp Glu Leu Val
545                 550                 555                 560

Arg Cys Ala Val Asp Ala Ala Thr Ala Tyr Glu Asn Ile Leu Asn Ala
                565                 570                 575

Ile Lys Ala Ala Glu Asp Ala Ala Asn Arg Ala Ala Ser Ala Ser Glu
            580                 585                 590

Ser Ala Leu Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Lys Ala Lys
        595                 600                 605

Thr Leu Ser Ser Asn Ser Asp Lys Leu Leu Asn Glu Ala Lys Met Thr
    610                 615                 620

Gln Lys Lys Leu Lys Gln Glu Val Ser Pro Ala Leu Asn Asn Leu Gln
625                 630                 635                 640

Gln Thr Leu Asn Ile Val Thr Val Gln Lys Glu Val Ile Asp Thr Asn
                645                 650                 655

Leu Thr Thr Leu Arg Asp Gly Leu His Gly Ile Gln Arg Gly Asp Ile
            660                 665                 670

Asp Ala Met Ile Ser Ser Ala Lys Ser Met Val Arg Lys Ala Asn Asp
        675                 680                 685

Ile Thr Asp Glu Val Leu Asp Gly Leu Asn Pro Ile Gln Thr Asp Val
    690                 695                 700

Glu Arg Ile Lys Asp Thr Tyr Gly Arg Thr Gln Asn Glu Asp Phe Lys
705                 710                 715                 720

Lys Ala Leu Thr Asp Ala Asp Asn Ser Val Asn Lys Leu Thr Asn Lys
                725                 730                 735
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Leu Pro Asp Leu Trp Arg Lys Ile Glu Ser Ile Asn Gln Gln Leu Leu
            740                 745                 750

Pro Leu Gly Asn Ile Ser Asp Asn Met Asp Arg Ile Arg Glu Leu Ile
        755                 760                 765

Gln Gln Ala Arg Asp Ala Ala Ser Lys Val Ala Val Pro Met Arg Phe
    770                 775                 780

Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu Asp
785                 790                 795                 800

Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asn Ser
                805                 810                 815

Arg Glu Asn Gly Gly Thr Glu Asn Met Phe Val Met Tyr Leu Gly Asn
            820                 825                 830

Lys Asp Ala Ser Arg Asp Tyr Ile Gly Met Ala Val Val Asp Gly Gln
        835                 840                 845

Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Leu Gln Val
    850                 855                 860

Asp Gln Ile Leu Thr Lys Ser Glu Thr Lys Glu Ala Val Met Asp Arg
865                 870                 875                 880

Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Arg Leu Asn Tyr Thr Lys
                885                 890                 895

Gly Ala Thr Ser Ser Lys Pro Glu Thr Pro Gly Val Tyr Asp Met Asp
            900                 905                 910

Gly Arg Asn Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asn Val Val
        915                 920                 925

Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Lys Leu Pro Ser Arg Leu
    930                 935                 940

Ser Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn Glu
945                 950                 955                 960

Asn Val Leu Ser Leu Tyr Asn Phe Lys Lys Thr Phe Asn Leu Asn Thr
                965                 970                 975

Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys Asn
            980                 985                 990

Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Val Pro Thr Gln Pro His Ala
        995                1000                1005

Pro Ile Pro Thr Phe Gly Gln Thr Ile Gln Thr Thr Val Asp Arg Gly
   1010                1015                1020

Leu Leu Phe Phe Ala Glu Asn Gly Asp Arg Phe Ile Ser Leu Asn Ile
025                1030                1035                1040

Glu Asp Gly Lys Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Leu Pro
               1045                1050                1055
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Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn Gly Arg Asp His Ser
1060 1065 1070

Ile Gln Ile Lys Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn Val
1075 1080 1085

Asp Val Gln Asn Thr Ile Ile Asp Gly Glu Val Phe Asp Phe Ser Thr
1090 1095 1100

Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn Ile
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Ser Thr Pro Ala Phe Arg Gly Cys Met Lys Asn Leu Lys Lys Thr Ser
1125 1130 1135

Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys Ser
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Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe Ser Arg Gly Gly Gln
1155 1160 1165

Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr Asp His Leu Gln Ala
1170 1175 1180

Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Ile Leu Leu Asp His
185 1190 1195 1200

Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu Glu Asp Gly Tyr Ile
1205 1210 1215

Glu Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile Phe Lys Ser Pro Gln
1220 1225 1230

Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser Val Ile Ser Asp Asn
1235 1240 1245

Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu Leu Arg Asn Ser Lys
1250 1255 1260

Arg Leu Lys His Ile Ser Ser Ser Arg Gln Ser Leu Arg Leu Gly Gly
265 1270 1275 1280

Ser Asn Phe Glu Gly Cys Ile Ser Asn Val Phe Val Gln Arg Leu Ser
1285 1290 1295

Leu Ser Pro Glu Val Leu Asp Leu Thr Ser Asn Ser Leu Lys Arg Asp
1300 1305 1310

Val Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met Leu
1315 1320 1325

Leu Lys Gly Ser Thr Arg Phe Asn Lys Thr Lys Thr Phe Arg Ile Asn
1330 1335 1340

Gln Leu Leu Gln Asp Thr Pro Val Ala Ser Pro Arg Ser Val Lys Val
345 1350 1355 1360

Trp Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr Gln Ala Asn His Gly
1365 1370 1375

Ala Leu Gln Phe Gly Asp Ile Pro Thr Ser His Leu Leu Phe Lys Leu

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          1380                1385                1390

Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ala Val Asp Met Gln
       1395                1400                1405

Thr Thr Ser Ser Arg Gly Leu Val Phe His Thr Gly Thr Lys Asn Ser
   1410                1415                1420

Phe Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu Val Phe Ala Leu Gly
425                1430                1435                1440

Thr Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys Glu Lys Cys Asn Asp
               1445                1450                1455

Gly Lys Trp His Thr Val Val Phe Gly His Asp Gly Glu Lys Gly Arg
           1460                1465                1470

Leu Val Val Asp Gly Leu Arg Ala Arg Glu Gly Ser Leu Pro Gly Asn
       1475                1480                1485

Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu Gly Ser Pro Pro Ser
   1490                1495                1500

Gly Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe Val Gly Cys Leu Lys
505                1510                1515                1520

Asn Phe Gln Leu Asp Ser Lys Pro Leu Tyr Thr Pro Ser Ser Ser Phe
               1525                1530                1535

Gly Val Ser Ser Cys Leu Gly Gly Pro Leu Glu Lys Gly Ile Tyr Phe
           1540                1545                1550

Ser Glu Glu Gly Gly His Val Val Leu Ala His Ser Val Leu Leu Gly
       1555                1560                1565

Pro Glu Phe Lys Leu Val Phe Ser Ile Arg Pro Arg Ser Leu Thr Gly
   1570                1575                1580

Ile Leu Ile His Ile Gly Ser Gln Pro Gly Lys His Leu Cys Val Tyr
585                1590                1595                1600

Leu Glu Ala Gly Lys Val Thr Ala Ser Met Asp Ser Gly Ala Gly Gly
               1605                1610                1615

Thr Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Gln Trp
           1620                1625                1630

His Ser Val Ala Val Thr Ile Lys Gln His Ile Leu His Leu Glu Leu
       1635                1640                1645

Asp Thr Asp Ser Ser Tyr Thr Ala Gly Gln Ile Pro Phe Pro Pro Ala
   1650                1655                1660

Ser Thr Gln Glu Pro Leu His Leu Gly Gly Ala Pro Ala Asn Leu Thr
665                1670                1675                1680

Thr Leu Arg Ile Pro Val Trp Lys Ser Phe Phe Gly Cys Leu Arg Asn
               1685                1690                1695

Ile His Val Asn His Ile Pro Val Pro Val Thr Glu Ala Leu Glu Val
           1700                1705                1710
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Gln Gly Pro Val Ser Leu Asn Gly Cys Pro Asp Gln
       1715                1720


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  1               5                  10                  15

gcg agt tat gtg gag ttt aga ccc agc cag ggt tgt agc cct gga tac   96
Ala Ser Tyr Val Glu Phe Arg Pro Ser Gln Gly Cys Ser Pro Gly Tyr
             20                  25                  30

tat cgg gat cat aaa ggc ttg tat acc gga cgg tgt gtt ccc tgc aat   144
Tyr Arg Asp His Lys Gly Leu Tyr Thr Gly Arg Cys Val Pro Cys Asn
         35                  40                  45

tgc aac gga cat tca aat caa tgc cag gat ggc tca ggc ata tgt gtt   192
Cys Asn Gly His Ser Asn Gln Cys Gln Asp Gly Ser Gly Ile Cys Val
     50                  55                  60

aac tgt cag cac aac acc gcg gga gag cac tgt gaa cgc tgc cag gag   240
Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Gln Glu
 65                  70                  75                  80

ggc tac tat ggc aac gcc gtc cac gga tcc tgc agg gcc tgc cca tgt   288
Gly Tyr Tyr Gly Asn Ala Val His Gly Ser Cys Arg Ala Cys Pro Cys
                 85                  90                  95

cct cac act aac agc ttt gcc act ggc tgt gtg gtg aat ggg gga gac   336
Pro His Thr Asn Ser Phe Ala Thr Gly Cys Val Val Asn Gly Gly Asp
            100                 105                 110

gtg cgg tgc tcc tgc aaa gct ggg tac aca gga aca cag tgt gaa agg   384
Val Arg Cys Ser Cys Lys Ala Gly Tyr Thr Gly Thr Gln Cys Glu Arg
        115                 120                 125

tgt gca ccg gga tat ttc ggg aat ccc cag aaa ttc gga ggt agc tgc   432
Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys
    130                 135                 140

caa cca tgc agt tgt aac agc aat ggc cag ctg ggc agc tgt cat ccc   480
Gln Pro Cys Ser Cys Asn Ser Asn Gly Gln Leu Gly Ser Cys His Pro
145                 150                 155                 160

ctg act gga gac tgc ata aac caa gaa ccc aaa gat agc agc cct gca   528
Leu Thr Gly Asp Cys Ile Asn Gln Glu Pro Lys Asp Ser Ser Pro Ala
                165                 170                 175

gaa gaa tgt gat gat tgc gac agc tgt gtg atg acc ctc ctg aac gac   576
Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp
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            180                 185                 190

ctg gcc acc atg ggc gag cag ctc cgc ctg gtc aag tct cag ctg cag   624
Leu Ala Thr Met Gly Glu Gln Leu Arg Leu Val Lys Ser Gln Leu Gln
        195                 200                 205

ggc ctg agt gcc agc gca ggg ctt ctg gag cag atg agg cac atg gag   672
Gly Leu Ser Ala Ser Ala Gly Leu Leu Glu Gln Met Arg His Met Glu
    210                 215                 220

acc cag gcc aag gac ctg agg aat cag ttg ctc aac tac cgt tct gcc   720
Thr Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Asn Tyr Arg Ser Ala
225                 230                 235                 240

att tca aat cat gga tca aaa ata gaa ggc ctg gaa aga gaa ctg act   768
Ile Ser Asn His Gly Ser Lys Ile Glu Gly Leu Glu Arg Glu Leu Thr
                245                 250                 255

gat ttg aat caa gaa ttt gag act tta caa gaa aag gct caa gta aat   816
Asp Leu Asn Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn
            260                 265                 270

tcc aga aaa gca caa aca tta aac aac aat gtt aat cgg gca aca caa   864
Ser Arg Lys Ala Gln Thr Leu Asn Asn Asn Val Asn Arg Ala Thr Gln
        275                 280                 285

agc gca aaa gaa cta gat gtg aag att aaa aat gtc atc cgg aat gtg   912
Ser Ala Lys Glu Leu Asp Val Lys Ile Lys Asn Val Ile Arg Asn Val
    290                 295                 300

cac att ctt tta aag cag atc tct ggg aca gat gga gag gga aac aac   960
His Ile Leu Leu Lys Gln Ile Ser Gly Thr Asp Gly Glu Gly Asn Asn
305                 310                 315                 320

gtg cct tca ggt gac ttt tcc aga gag tgg gct gaa gcc cag cgc atg   1008
Val Pro Ser Gly Asp Phe Ser Arg Glu Trp Ala Glu Ala Gln Arg Met
                325                 330                 335

atg agg gaa ctg cgg aac agg aac ttt gga aag cac ctc aga gaa gca   1056
Met Arg Glu Leu Arg Asn Arg Asn Phe Gly Lys His Leu Arg Glu Ala
            340                 345                 350

gaa gct gat aaa agg gag tcg cag ctc ttg ctg aac cgg ata agg acc   1104
Glu Ala Asp Lys Arg Glu Ser Gln Leu Leu Leu Asn Arg Ile Arg Thr
        355                 360                 365

tgg cag aaa acc cac cag ggg gag aac aat ggg ctt gct aac agt atc   1152
Trp Gln Lys Thr His Gln Gly Glu Asn Asn Gly Leu Ala Asn Ser Ile
    370                 375                 380

cgg gat tct tta aat gaa tac gaa gcc aaa ctc agt gac ctt cgt gct   1200
Arg Asp Ser Leu Asn Glu Tyr Glu Ala Lys Leu Ser Asp Leu Arg Ala
385                 390                 395                 400

cgg ctg cag gag gca gct gcc caa gcc aag cag gca aat ggc ttg aac   1248
Arg Leu Gln Glu Ala Ala Ala Gln Ala Lys Gln Ala Asn Gly Leu Asn
                405                 410                 415

caa gaa aac gag aga gct ttg gga gcc att cag aga caa gtg aaa gaa   1296
Gln Glu Asn Glu Arg Ala Leu Gly Ala Ile Gln Arg Gln Val Lys Glu
            420                 425                 430
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ata aat tcc ctg cag agt gat ttc acc aag tat cta acc act gca gac   1344
Ile Asn Ser Leu Gln Ser Asp Phe Thr Lys Tyr Leu Thr Thr Ala Asp
        435                 440                 445

tca tct ttg ttg caa acc aac att gcg ctg cag ctg atg gag aaa agc   1392
Ser Ser Leu Leu Gln Thr Asn Ile Ala Leu Gln Leu Met Glu Lys Ser
    450                 455                 460

cag aag gaa tat gaa aaa tta gct gcc agt tta aat gaa gca aga caa   1440
Gln Lys Glu Tyr Glu Lys Leu Ala Ala Ser Leu Asn Glu Ala Arg Gln
465                 470                 475                 480

gaa cta agt gac aaa gta aga gaa ctt tcc aga tct gct ggc aaa aca   1488
Glu Leu Ser Asp Lys Val Arg Glu Leu Ser Arg Ser Ala Gly Lys Thr
                485                 490                 495

tcc ctt gtg gag gag gca gaa aag cac gcg cgg tcc tta caa gag ctg   1536
Ser Leu Val Glu Glu Ala Glu Lys His Ala Arg Ser Leu Gln Glu Leu
            500                 505                 510

gca aag cag ctg gaa gag atc aag aga aac gcc agc ggg gat gag ctg   1584
Ala Lys Gln Leu Glu Glu Ile Lys Arg Asn Ala Ser Gly Asp Glu Leu
        515                 520                 525

gtg cgc tgt gct gtg gat gcc gcc acc gcc tac gag aac atc ctc aat   1632
Val Arg Cys Ala Val Asp Ala Ala Thr Ala Tyr Glu Asn Ile Leu Asn
    530                 535                 540

gcc atc aaa gcg gcc gag gac gca gcc aac agg gct gcc agt gca tct   1680
Ala Ile Lys Ala Ala Glu Asp Ala Ala Asn Arg Ala Ala Ser Ala Ser
545                 550                 555                 560

gaa tct gcc ctc cag aca gtg ata aag gaa gat ctg cca aga aaa gct   1728
Glu Ser Ala Leu Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Lys Ala
                565                 570                 575

aaa acc ctg agt tcc aac agt gat aaa ctg tta aat gaa gcc aag atg   1776
Lys Thr Leu Ser Ser Asn Ser Asp Lys Leu Leu Asn Glu Ala Lys Met
            580                 585                 590

aca caa aag aag cta aag caa gaa gtc agt cca gct ctc aac aac cta   1824
Thr Gln Lys Lys Leu Lys Gln Glu Val Ser Pro Ala Leu Asn Asn Leu
        595                 600                 605

cag caa acc ctg aat att gtg aca gtt cag aaa gaa gtg ata gac acc   1872
Gln Gln Thr Leu Asn Ile Val Thr Val Gln Lys Glu Val Ile Asp Thr
    610                 615                 620

aat ctc aca act ctc cga gat ggt ctt cat ggg ata cag aga ggt gat   1920
Asn Leu Thr Thr Leu Arg Asp Gly Leu His Gly Ile Gln Arg Gly Asp
625                 630                 635                 640

att gat gct atg atc agt agt gca aag agc atg gtc aga aag gcc aac   1968
Ile Asp Ala Met Ile Ser Ser Ala Lys Ser Met Val Arg Lys Ala Asn
                645                 650                 655

gac atc aca gat gag gtt ctg gat ggg ctc aac ccc atc cag aca gat   2016
Asp Ile Thr Asp Glu Val Leu Asp Gly Leu Asn Pro Ile Gln Thr Asp
            660                 665                 670
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gtg gaa aga att aag gac acc tat ggg agg aca cag aac gaa gac ttc   2064
Val Glu Arg Ile Lys Asp Thr Tyr Gly Arg Thr Gln Asn Glu Asp Phe
        675                 680                 685

aaa aag gct ctg act gat gca gat aac tcg gtg aat aag tta acc aac   2112
Lys Lys Ala Leu Thr Asp Ala Asp Asn Ser Val Asn Lys Leu Thr Asn
    690                 695                 700

aaa cta cct gat ctt tgg cgc aag att gaa agt atc aac caa cag ctg   2160
Lys Leu Pro Asp Leu Trp Arg Lys Ile Glu Ser Ile Asn Gln Gln Leu
705                 710                 715                 720

ttg ccc ttg gga aac atc tct gac aac atg gac aga ata cga gaa cta   2208
Leu Pro Leu Gly Asn Ile Ser Asp Asn Met Asp Arg Ile Arg Glu Leu
                725                 730                 735

att cag cag gcc aga gat gct gcc agt aag gtt gct gtc ccc atg agg   2256
Ile Gln Gln Ala Arg Asp Ala Ala Ser Lys Val Ala Val Pro Met Arg
            740                 745                 750

ttc aat ggt aaa tct gga gtc gaa gtc cga ctg cca aat gac ctg gaa   2304
Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu
        755                 760                 765

gat ttg aaa gga tat aca tct ctg tcc ttg ttt ctc caa agg ccc aac   2352
Asp Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asn
    770                 775                 780

tca aga gaa aat ggg ggt act gag aat atg ttt gtg atg tac ctt gga   2400
Ser Arg Glu Asn Gly Gly Thr Glu Asn Met Phe Val Met Tyr Leu Gly
785                 790                 795                 800

aat aaa gat gcc tcc cgg gac tac atc ggc atg gca gtt gtg gat ggc   2448
Asn Lys Asp Ala Ser Arg Asp Tyr Ile Gly Met Ala Val Val Asp Gly
                805                 810                 815

cag ctc acc tgt gtc tac aac ctg ggg gac cgt gag gct gaa ctc caa   2496
Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Leu Gln
            820                 825                 830

gtg gac cag atc ttg acc aag agt gag act aag gag gca gtt atg gat   2544
Val Asp Gln Ile Leu Thr Lys Ser Glu Thr Lys Glu Ala Val Met Asp
        835                 840                 845

cgg gtg aaa ttt cag aga att tat cag ttt gca agg ctt aat tac acc   2592
Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Arg Leu Asn Tyr Thr
    850                 855                 860

aaa gga gcc aca tcc agt aaa cca gaa aca ccc gga gtc tat gac atg   2640
Lys Gly Ala Thr Ser Ser Lys Pro Glu Thr Pro Gly Val Tyr Asp Met
865                 870                 875                 880

gat ggt aga aat agc aat aca ctc ctt aat ttg gat cct gaa aat gtt   2688
Asp Gly Arg Asn Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asn Val
                885                 890                 895

gta ttt tat gtt gga ggt tac cca cct gat ttt aaa ctt ccc agt cga   2736
Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Lys Leu Pro Ser Arg
            900                 905                 910

cta agt ttc cct cca tac aaa ggt tgt att gaa tta gat gac ctc aat   2784
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Leu Ser Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn
        915                 920                 925

gaa aat gtt ctg agc ttg tac aac ttc aaa aaa aca ttc aat ctc aac   2832
Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Lys Thr Phe Asn Leu Asn
    930                 935                 940

aca act gaa gtg gag cct tgt aga agg agg aag gaa gag tca gac aaa   2880
Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys
945                 950                 955                 960

aat tat ttt gaa ggt acg ggc tat gct cga gtt cca act caa cca cat   2928
Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Val Pro Thr Gln Pro His
                965                 970                 975

gct ccc atc cca acc ttt gga cag aca att cag acc acc gtg gat aga   2976
Ala Pro Ile Pro Thr Phe Gly Gln Thr Ile Gln Thr Thr Val Asp Arg
            980                 985                 990

ggc ttg ctg ttc ttt gca gaa aac ggg gat cgc ttc ata tct cta aat   3024
Gly Leu Leu Phe Phe Ala Glu Asn Gly Asp Arg Phe Ile Ser Leu Asn
        995                1000                1005

ata gaa gat ggc aag ctc atg gtg aga tac aaa ctg aat tca gag cta   3072
Ile Glu Asp Gly Lys Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Leu
   1010                1015                1020

cca aaa gag aga gga gtt gga gac gcc ata aac aac ggc aga gac cat   3120
Pro Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn Gly Arg Asp His
1025                1030                1035                1040

tcg att cag atc aaa att gga aaa ctc caa aag cgt atg tgg ata aat   3168
Ser Ile Gln Ile Lys Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn
               1045                1050                1055

gtg gac gtt caa aac act ata att gat ggt gaa gta ttt gat ttc agc   3216
Val Asp Val Gln Asn Thr Ile Ile Asp Gly Glu Val Phe Asp Phe Ser
           1060                1065                1070

aca tat tat ctg gga gga att cca att gca atc agg gaa aga ttt aac   3264
Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn
       1075                1080                1085

att tct acg cct gct ttc cga ggc tgc atg aaa aat ttg aag aaa acc   3312
Ile Ser Thr Pro Ala Phe Arg Gly Cys Met Lys Asn Leu Lys Lys Thr
   1090                1095                1100

agt ggt gtc gtt aga ttg aat gat act gtg gga gta acc aaa aag tgc   3360
Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys
1105                1110                1115                1120

tcg gaa gac tgg aag ctt gtg cga tct gcc tca ttc tcc aga gga gga   3408
Ser Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe Ser Arg Gly Gly
               1125                1130                1135

caa ttg agt ttc act gat ttg ggc tta cca cct act gac cac ctc cag   3456
Gln Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr Asp His Leu Gln
           1140                1145                1150

gcc tca ttt gga ttt cag acc ttt caa ccc agt ggc ata tta tta gat   3504
Ala Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Ile Leu Leu Asp
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cat cag aca tgg aca agg aac ctg cag gtc act ctg gaa gat ggt tac   3552
His Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu Glu Asp Gly Tyr
   1170                1175                1180

att gaa ttg agc acc agc gat agc ggc ggc cca att ttt aaa tct cca   3600
Ile Glu Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile Phe Lys Ser Pro
1185                1190                1195                1200

cag acg tat atg gat ggt tta ctg cat tat gta tct gta ata agc gac   3648
Gln Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser Val Ile Ser Asp
                1205                1210                1215

aac tct gga cta cgg ctt ctc atc gat gac cag ctt ctg aga aat agc   3696
Asn Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu Leu Arg Asn Ser
           1220                1225                1230

aaa agg cta aaa cac att tca agt tcc cgg cag tct ctg cgt ctg ggc   3744
Lys Arg Leu Lys His Ile Ser Ser Ser Arg Gln Ser Leu Arg Leu Gly
       1235                1240                1245

ggg agc aat ttt gag ggt tgt att agc aat gtt ttt gtc cag agg tta   3792
Gly Ser Asn Phe Glu Gly Cys Ile Ser Asn Val Phe Val Gln Arg Leu
   1250                1255                1260

tca ctg agt cct gaa gtc cta gat ttg acc agt aac tct ctc aag aga   3840
Ser Leu Ser Pro Glu Val Leu Asp Leu Thr Ser Asn Ser Leu Lys Arg
1265                1270                1275                1280

gat gtg tcc ctg gga ggc tgc agt tta aac aaa cca cct ttt cta atg   3888
Asp Val Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met
                1285                1290                1295

ttg ctt aaa ggt tct acc agg ttt aac aag acc aag act ttt cgt atc   3936
Leu Leu Lys Gly Ser Thr Arg Phe Asn Lys Thr Lys Thr Phe Arg Ile
           1300                1305                1310

aac cag ctg ttg cag gac aca cca gtg gcc tcc cca agg agc gtg aag   3984
Asn Gln Leu Leu Gln Asp Thr Pro Val Ala Ser Pro Arg Ser Val Lys
       1315                1320                1325

gtg tgg caa gat gct tgc tca cca ctt ccc aag acc cag gcc aat cat   4032
Val Trp Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr Gln Ala Asn His
   1330                1335                1340

gga gcc ctc cag ttt ggg gac att ccc acc agc cac ttg cta ttc aag   4080
Gly Ala Leu Gln Phe Gly Asp Ile Pro Thr Ser His Leu Leu Phe Lys
1345                1350                1355                1360

ctt cct cag gag ctg ctg aaa ccc agg tca cag ttt gct gtg gac atg   4128
Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ala Val Asp Met
                1365                1370                1375

cag aca aca tcc tcc aga gga ctg gtg ttt cac acg ggc act aag aac   4176
Gln Thr Thr Ser Ser Arg Gly Leu Val Phe His Thr Gly Thr Lys Asn
           1380                1385                1390

tcc ttt atg gct ctt tat ctt tca aaa gga cgt ctg gtc ttt gca ctg   4224
Ser Phe Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu Val Phe Ala Leu
       1395                1400                1405
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ggg aca gat ggg aaa aaa ttg agg atc aaa agc aag gag aaa tgc aat   4272
Gly Thr Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys Glu Lys Cys Asn
   1410                1415                1420

gat ggg aaa tgg cac acg gtg gtg ttt ggc cat gat ggg gaa aag ggg   4320
Asp Gly Lys Trp His Thr Val Val Phe Gly His Asp Gly Glu Lys Gly
1425                1430                1435                1440

cgc ttg gtt gtg gat gga ctg agg gcc cgg gag gga agt ttg cct gga   4368
Arg Leu Val Val Asp Gly Leu Arg Ala Arg Glu Gly Ser Leu Pro Gly
               1445                1450                1455

aac tcc acc atc agc atc aga gcg cca gtt tac ctg gga tca cct cca   4416
Asn Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu Gly Ser Pro Pro
           1460                1465                1470

tca ggg aaa cca aag agc ctc ccc aca aac agc ttt gtg gga tgc ctg   4464
Ser Gly Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe Val Gly Cys Leu
       1475                1480                1485

aag aac ttt cag ctg gat tca aaa ccc ttg tat acc cct tct tca agc   4512
Lys Asn Phe Gln Leu Asp Ser Lys Pro Leu Tyr Thr Pro Ser Ser Ser
   1490                1495                1500

ttc ggg gtg tct tcc tgc ttg ggt ggt cct ttg gag aaa ggc att tat   4560
Phe Gly Val Ser Ser Cys Leu Gly Gly Pro Leu Glu Lys Gly Ile Tyr
1505                1510                1515                1520

ttc tct gaa gaa gga ggt cat gtc gtc ttg gct cac tct gta ttg ttg   4608
Phe Ser Glu Glu Gly Gly His Val Val Leu Ala His Ser Val Leu Leu
               1525                1530                1535

ggg cca gaa ttt aag ctt gtt ttc agc atc cgc cca aga agt ctc act   4656
Gly Pro Glu Phe Lys Leu Val Phe Ser Ile Arg Pro Arg Ser Leu Thr
           1540                1545                1550

ggg atc cta ata cac atc gga agt cag ccc ggg aag cac tta tgt gtt   4704
Gly Ile Leu Ile His Ile Gly Ser Gln Pro Gly Lys His Leu Cys Val
       1555                1560                1565

tac ctg gag gca gga aag gtc acg gcc tct atg gac agt ggg gca ggt   4752
Tyr Leu Glu Ala Gly Lys Val Thr Ala Ser Met Asp Ser Gly Ala Gly
   1570                1575                1580

ggg acc tca acg tcg gtc aca cca aag cag tct ctg tgt gat gga cag   4800
Gly Thr Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Gln
1585                1590                1595                1600

tgg cac tcg gtg gca gtc acc ata aaa caa cac atc ctg cac ctg gaa   4848
Trp His Ser Val Ala Val Thr Ile Lys Gln His Ile Leu His Leu Glu
               1605                1610                1615

ctg gac aca gac agt agc tac aca gct gga cag atc ccc ttc cca cct   4896
Leu Asp Thr Asp Ser Ser Tyr Thr Ala Gly Gln Ile Pro Phe Pro Pro
           1620                1625                1630

gcc agc act caa gag cca cta cac ctt gga ggt gct cca gcc aat ttg   4944
Ala Ser Thr Gln Glu Pro Leu His Leu Gly Gly Ala Pro Ala Asn Leu
       1635                1640                1645
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acg aca ctg agg atc cct gtg tgg aaa tca ttc ttt ggc tgt ctg agg   4992
Thr Thr Leu Arg Ile Pro Val Trp Lys Ser Phe Phe Gly Cys Leu Arg
   1650                1655                1660

aat att cat gtc aat cac atc cct gtc cct gtc act gaa gcc ttg gaa   5040
Asn Ile His Val Asn His Ile Pro Val Pro Val Thr Glu Ala Leu Glu
1665               1670                1675                1680

gtc cag ggg cct gtc agt ctg aat ggt tgt cct gac cag taacccaagc    5089
Val Gln Gly Pro Val Ser Leu Asn Gly Cys Pro Asp Gln
               1685                1690

ctatttcaca gcaaggaaat tcaccttcaa aagcactgat tacccaatgc acctccctcc 5149

ccagctcgag atcattcttc a                                          5170
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<213> Homo sapiens

<400> 4

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Gln Gln Arg Val Pro Phe Leu Gln Pro Pro Gly Gln Ser Gln Leu Gln
  1               5                  10                  15

Ala Ser Tyr Val Glu Phe Arg Pro Ser Gln Gly Cys Ser Pro Gly Tyr
             20                  25                  30

Tyr Arg Asp His Lys Gly Leu Tyr Thr Gly Arg Cys Val Pro Cys Asn
         35                  40                  45

Cys Asn Gly His Ser Asn Gln Cys Gln Asp Gly Ser Gly Ile Cys Val
     50                  55                  60

Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Gln Glu
 65                  70                  75                  80

Gly Tyr Tyr Gly Asn Ala Val His Gly Ser Cys Arg Ala Cys Pro Cys
                 85                  90                  95

Pro His Thr Asn Ser Phe Ala Thr Gly Cys Val Val Asn Gly Gly Asp
            100                 105                 110

Val Arg Cys Ser Cys Lys Ala Gly Tyr Thr Gly Thr Gln Cys Glu Arg
        115                 120                 125

Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys
    130                 135                 140

Gln Pro Cys Ser Cys Asn Ser Asn Gly Gln Leu Gly Ser Cys His Pro
145                 150                 155                 160

Leu Thr Gly Asp Cys Ile Asn Gln Glu Pro Lys Asp Ser Ser Pro Ala
                165                 170                 175

Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp
            180                 185                 190

Leu Ala Thr Met Gly Glu Gln Leu Arg Leu Val Lys Ser Gln Leu Gln
        195                 200                 205
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Gly Leu Ser Ala Ser Ala Gly Leu Leu Glu Gln Met Arg His Met Glu
    210                 215                 220

Thr Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Asn Tyr Arg Ser Ala
225                 230                 235                 240

Ile Ser Asn His Gly Ser Lys Ile Glu Gly Leu Glu Arg Glu Leu Thr
                245                 250                 255

Asp Leu Asn Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn
            260                 265                 270

Ser Arg Lys Ala Gln Thr Leu Asn Asn Asn Val Asn Arg Ala Thr Gln
        275                 280                 285

Ser Ala Lys Glu Leu Asp Val Lys Ile Lys Asn Val Ile Arg Asn Val
    290                 295                 300

His Ile Leu Leu Lys Gln Ile Ser Gly Thr Asp Gly Glu Gly Asn Asn
305                 310                 315                 320

Val Pro Ser Gly Asp Phe Ser Arg Glu Trp Ala Glu Ala Gln Arg Met
                325                 330                 335

Met Arg Glu Leu Arg Asn Arg Asn Phe Gly Lys His Leu Arg Glu Ala
            340                 345                 350

Glu Ala Asp Lys Arg Glu Ser Gln Leu Leu Leu Asn Arg Ile Arg Thr
        355                 360                 365

Trp Gln Lys Thr His Gln Gly Glu Asn Asn Gly Leu Ala Asn Ser Ile
    370                 375                 380

Arg Asp Ser Leu Asn Glu Tyr Glu Ala Lys Leu Ser Asp Leu Arg Ala
385                 390                 395                 400

Arg Leu Gln Glu Ala Ala Ala Gln Ala Lys Gln Ala Asn Gly Leu Asn
                405                 410                 415

Gln Glu Asn Glu Arg Ala Leu Gly Ala Ile Gln Arg Gln Val Lys Glu
            420                 425                 430

Ile Asn Ser Leu Gln Ser Asp Phe Thr Lys Tyr Leu Thr Thr Ala Asp
        435                 440                 445

Ser Ser Leu Leu Gln Thr Asn Ile Ala Leu Gln Leu Met Glu Lys Ser
    450                 455                 460

Gln Lys Glu Tyr Glu Lys Leu Ala Ala Ser Leu Asn Glu Ala Arg Gln
465                 470                 475                 480

Glu Leu Ser Asp Lys Val Arg Glu Leu Ser Arg Ser Ala Gly Lys Thr
                485                 490                 495

Ser Leu Val Glu Glu Ala Glu Lys His Ala Arg Ser Leu Gln Glu Leu
            500                 505                 510

Ala Lys Gln L u Glu Glu Ile Lys Arg Asn Ala S r Gly Asp Glu Leu
        515                 520                 525
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Val Arg Cys Ala Val Asp Ala Ala Thr Ala Tyr Glu Asn Ile Leu Asn
    530                 535                 540

Ala Ile Lys Ala Ala Glu Asp Ala Ala Asn Arg Ala Ala Ser Ala Ser
545                 550                 555                 560

Glu Ser Ala Leu Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Lys Ala
                565                 570                 575

Lys Thr Leu Ser Ser Asn Ser Asp Lys Leu Leu Asn Glu Ala Lys Met
            580                 585                 590

Thr Gln Lys Lys Leu Lys Gln Glu Val Ser Pro Ala Leu Asn Asn Leu
        595                 600                 605

Gln Gln Thr Leu Asn Ile Val Thr Val Gln Lys Glu Val Ile Asp Thr
    610                 615                 620

Asn Leu Thr Thr Leu Arg Asp Gly Leu His Gly Ile Gln Arg Gly Asp
625                 630                 635                 640

Ile Asp Ala Met Ile Ser Ser Ala Lys Ser Met Val Arg Lys Ala Asn
                645                 650                 655

Asp Ile Thr Asp Glu Val Leu Asp Gly Leu Asn Pro Ile Gln Thr Asp
            660                 665                 670

Val Glu Arg Ile Lys Asp Thr Tyr Gly Arg Thr Gln Asn Glu Asp Phe
        675                 680                 685

Lys Lys Ala Leu Thr Asp Ala Asp Asn Ser Val Asn Lys Leu Thr Asn
    690                 695                 700

Lys Leu Pro Asp Leu Trp Arg Lys Ile Glu Ser Ile Asn Gln Gln Leu
705                 710                 715                 720

Leu Pro Leu Gly Asn Ile Ser Asp Asn Met Asp Arg Ile Arg Glu Leu
                725                 730                 735

Ile Gln Gln Ala Arg Asp Ala Ala Ser Lys Val Ala Val Pro Met Arg
            740                 745                 750

Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu
        755                 760                 765

Asp Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asn
    770                 775                 780

Ser Arg Glu Asn Gly Gly Thr Glu Asn Met Phe Val Met Tyr Leu Gly
785                 790                 795                 800

Asn Lys Asp Ala Ser Arg Asp Tyr Ile Gly Met Ala Val Val Asp Gly
                805                 810                 815

Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Leu Gln
            820                 825                 830

Val Asp Gln Ile Leu Thr Lys Ser Glu Thr Lys Glu Ala Val Met Asp
        835                 840                 845

Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Arg Leu Asn Tyr Thr
```

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    850                 855                 860

Lys Gly Ala Thr Ser Ser Lys Pro Glu Thr Pro Gly Val Tyr Asp Met
865                 870                 875                 880

Asp Gly Arg Asn Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asn Val
                885                 890                 895

Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Lys Leu Pro Ser Arg
            900                 905                 910

Leu Ser Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn
        915                 920                 925

Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Lys Thr Phe Asn Leu Asn
    930                 935                 940

Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys
945                 950                 955                 960

Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Val Pro Thr Gln Pro His
                965                 970                 975

Ala Pro Ile Pro Thr Phe Gly Gln Thr Ile Gln Thr Thr Val Asp Arg
            980                 985                 990

Gly Leu Leu Phe Phe Ala Glu Asn Gly Asp Arg Phe Ile Ser Leu Asn
        995                1000                1005

Ile Glu Asp Gly Lys Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Leu
   1010                1015                1020

Pro Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn Gly Arg Asp His
1025                1030                1035                1040

Ser Ile Gln Ile Lys Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn
                1045                1050                1055

Val Asp Val Gln Asn Thr Ile Ile Asp Gly Glu Val Phe Asp Phe Ser
            1060                1065                1070

Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn
        1075                1080                1085

Ile Ser Thr Pro Ala Phe Arg Gly Cys Met Lys Asn Leu Lys Lys Thr
   1090                1095                1100

Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys
1105                1110                1115                1120

Ser Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe Ser Arg Gly Gly
                1125                1130                1135

Gln Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr Asp His Leu Gln
            1140                1145                1150

Ala Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Ile Leu Leu Asp
        1155                1160                1165

His Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu Glu Asp Gly Tyr
   1170                1175                1180
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Ile Glu Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile Phe Lys Ser Pro
1185                1190                1195                1200

Gln Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser Val Ile Ser Asp
                1205                1210                1215

Asn Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu Leu Arg Asn Ser
            1220                1225                1230

Lys Arg Leu Lys His Ile Ser Ser Ser Arg Gln Ser Leu Arg Leu Gly
        1235                1240                1245

Gly Ser Asn Phe Glu Gly Cys Ile Ser Asn Val Phe Val Gln Arg Leu
    1250                1255                1260

Ser Leu Ser Pro Glu Val Leu Asp Leu Thr Ser Asn Ser Leu Lys Arg
1265                1270                1275                1280

Asp Val Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met
                1285                1290                1295

Leu Leu Lys Gly Ser Thr Arg Phe Asn Lys Thr Lys Thr Phe Arg Ile
            1300                1305                1310

Asn Gln Leu Leu Gln Asp Thr Pro Val Ala Ser Pro Arg Ser Val Lys
        1315                1320                1325

Val Trp Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr Gln Ala Asn His
    1330                1335                1340

Gly Ala Leu Gln Phe Gly Asp Ile Pro Thr Ser His Leu Leu Phe Lys
1345                1350                1355                1360

Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ala Val Asp Met
                1365                1370                1375

Gln Thr Thr Ser Ser Arg Gly Leu Val Phe His Thr Gly Thr Lys Asn
            1380                1385                1390

Ser Phe Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu Val Phe Ala Leu
        1395                1400                1405

Gly Thr Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys Glu Lys Cys Asn
    1410                1415                1420

Asp Gly Lys Trp His Thr Val Val Phe Gly His Asp Gly Glu Lys Gly
1425                1430                1435                1440

Arg Leu Val Val Asp Gly Leu Arg Ala Arg Glu Gly Ser Leu Pro Gly
                1445                1450                1455

Asn Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu Gly Ser Pro Pro
            1460                1465                1470

Ser Gly Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe Val Gly Cys Leu
        1475                1480                1485

Lys Asn Phe Gln L u Asp Ser Lys Pro Leu Tyr Thr Pro Ser Ser Ser
    1490                1495                1500
```

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Phe Gly Val Ser Ser Cys Leu Gly Gly Pro Leu Glu Lys Gly Ile Tyr
1505                1510                1515                1520

Phe Ser Glu Glu Gly Gly His Val Val Leu Ala His Ser Val Leu Leu
                1525                1530                1535

Gly Pro Glu Phe Lys Leu Val Phe Ser Ile Arg Pro Arg Ser Leu Thr
            1540                1545                1550

Gly Ile Leu Ile His Ile Gly Ser Gln Pro Gly Lys His Leu Cys Val
        1555                1560                1565

Tyr Leu Glu Ala Gly Lys Val Thr Ala Ser Met Asp Ser Gly Ala Gly
    1570                1575                1580

Gly Thr Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Gln
1585                1590                1595                1600

Trp His Ser Val Ala Val Thr Ile Lys Gln His Ile Leu His Leu Glu
                1605                1610                1615

Leu Asp Thr Asp Ser Ser Tyr Thr Ala Gly Gln Ile Pro Phe Pro Pro
            1620                1625                1630

Ala Ser Thr Gln Glu Pro Leu His Leu Gly Gly Ala Pro Ala Asn Leu
        1635                1640                1645

Thr Thr Leu Arg Ile Pro Val Trp Lys Ser Phe Phe Gly Cys Leu Arg
    1650                1655                1660

Asn Ile His Val Asn His Ile Pro Val Pro Val Thr Glu Ala Leu Glu
1665                1670                1675                1680

Val Gln Gly Pro Val Ser Leu Asn Gly Cys Pro Asp Gln
                1685                1690
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Met Gly Trp Leu Trp Ile Phe Gly Ala Ala Leu Gly Gln Cys Leu Gly
  1               5                  10                  15

tac agt tca cag cag caa agg gtg cca ttt ctt cag cct ccc ggt caa   96
Tyr Ser Ser Gln Gln Gln Arg Val Pro Phe Leu Gln Pro Pro Gly Gln
             20                  25                  30

agt caa ctg caa gcg agt tat gtg gag ttt aga ccc agc cag ggt tgt   144
Ser Gln Leu Gln Ala Ser Tyr Val Glu Phe Arg Pro Ser Gln Gly Cys
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        35                  40                  45

agc cct gga tac tat cgg gat cat aaa ggc ttg tat acc gga cgg tgt   192
Ser Pro Gly Tyr Tyr Arg Asp His Lys Gly Leu Tyr Thr Gly Arg Cys
     50                  55                  60

gtt ccc tgc aat tgc aac gga cat tca aat caa tgc cag gat ggc tca   240
Val Pro Cys Asn Cys Asn Gly His Ser Asn Gln Cys Gln Asp Gly Ser
 65                  70                  75                  80

ggc ata tgt gtt aac tgt cag cac aac acc gcg gga gag cac tgt gaa   288
Gly Ile Cys Val Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu
                 85                  90                  95

cgc tgc cag gag ggc tac tat ggc aac gcc gtc cac gga tcc tgc agg   336
Arg Cys Gln Glu Gly Tyr Tyr Gly Asn Ala Val His Gly Ser Cys Arg
            100                 105                 110

gcc tgc cca tgt cct cac act aac agc ttt gcc act ggc tgt gtg gtg   384
Ala Cys Pro Cys Pro His Thr Asn Ser Phe Ala Thr Gly Cys Val Val
        115                 120                 125

aat ggg gga gac gtg cgg tgc tcc tgc aaa gct ggg tac aca gga aca   432
Asn Gly Gly Asp Val Arg Cys Ser Cys Lys Ala Gly Tyr Thr Gly Thr
    130                 135                 140

cag tgt gaa agg tgt gca ccg gga tat ttc ggg aat ccc cag aaa ttc   480
Gln Cys Glu Arg Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe
145                 150                 155                 160

gga ggt agc tgc caa cca tgc agt tgt aac agc aat ggc cag ctg ggc   528
Gly Gly Ser Cys Gln Pro Cys Ser Cys Asn Ser Asn Gly Gln Leu Gly
                165                 170                 175

agc tgt cat ccc ctg act gga gac tgc ata aac caa gaa ccc aaa gat   576
Ser Cys His Pro Leu Thr Gly Asp Cys Ile Asn Gln Glu Pro Lys Asp
            180                 185                 190

agc agc cct gca gaa gaa tgt gat gat tgc gac agc tgt gtg atg acc   624
Ser Ser Pro Ala Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr
        195                 200                 205

ctc ctg aac gac ctg gcc acc atg ggc gag cag ctc cgc ctg gtc aag   672
Leu Leu Asn Asp Leu Ala Thr Met Gly Glu Gln Leu Arg Leu Val Lys
    210                 215                 220

tct cag ctg cag ggc ctg agt gcc agc gca ggg ctt ctg gag cag atg   720
Ser Gln Leu Gln Gly Leu Ser Ala Ser Ala Gly Leu Leu Glu Gln Met
225                 230                 235                 240

agg cac atg gag acc cag gcc aag gac ctg agg aat cag ttg ctc aac   768
Arg His Met Glu Thr Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Asn
                245                 250                 255

tac cgt tct gcc att tca aat cat gga tca aaa ata gaa ggc ctg gaa   816
Tyr Arg Ser Ala Ile Ser Asn His Gly Ser Lys Ile Glu Gly Leu Glu
            260                 265                 270

aga gaa ctg act gat ttg aat caa gaa ttt gag act ttg caa gaa aag   864
Arg Glu Leu Thr Asp Leu Asn Gln Glu Phe Glu Thr Leu Gln Glu Lys
        275                 280                 285
```

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gct caa gta aat tcc aga aaa gca caa aca tta aac aac aat gtt aat   912
Ala Gln Val Asn Ser Arg Lys Ala Gln Thr Leu Asn Asn Asn Val Asn
    290                 295                 300

cgg gca aca caa agc gca aaa gaa ctg gat gtg aag att aaa aat gtc   960
Arg Ala Thr Gln Ser Ala Lys Glu Leu Asp Val Lys Ile Lys Asn Val
305                 310                 315                 320

atc cgg aat gtg cac att ctt tta aag cag atc tct ggg aca gat gga  1008
Ile Arg Asn Val His Ile Leu Leu Lys Gln Ile Ser Gly Thr Asp Gly
                325                 330                 335

gag gga aac aac gtg cct tca ggt gac ttt tcc aga gag tgg gct gaa  1056
Glu Gly Asn Asn Val Pro Ser Gly Asp Phe Ser Arg Glu Trp Ala Glu
            340                 345                 350

gcc cag cgc atg atg agg gaa ctg cgg aac agg aac ttt gga aag cac  1104
Ala Gln Arg Met Met Arg Glu Leu Arg Asn Arg Asn Phe Gly Lys His
        355                 360                 365

ctc aga gaa gca gaa gct gat aaa agg gag tcg cag ctc ttg ctg aac  1152
Leu Arg Glu Ala Glu Ala Asp Lys Arg Glu Ser Gln Leu Leu Leu Asn
    370                 375                 380

cgg ata agg acc tgg cag aaa acc cac cag ggg gag aac aat ggg ctt  1200
Arg Ile Arg Thr Trp Gln Lys Thr His Gln Gly Glu Asn Asn Gly Leu
385                 390                 395                 400

gct aac agt atc cgg gat tct tta aat gaa tac gaa gcc aaa ctc agt  1248
Ala Asn Ser Ile Arg Asp Ser Leu Asn Glu Tyr Glu Ala Lys Leu Ser
                405                 410                 415

gac ctt cgt gct cgg ctg cag gag gca gct gcc caa gcc aag cag gca  1296
Asp Leu Arg Ala Arg Leu Gln Glu Ala Ala Ala Gln Ala Lys Gln Ala
            420                 425                 430

aat ggc ttg aac caa gaa aac gag aga gct ttg gga gcc att cag aga  1344
Asn Gly Leu Asn Gln Glu Asn Glu Arg Ala Leu Gly Ala Ile Gln Arg
        435                 440                 445

caa gtg aaa gaa ata aat tcc ctg cag agt gat ttc acc aag tat cta  1392
Gln Val Lys Glu Ile Asn Ser Leu Gln Ser Asp Phe Thr Lys Tyr Leu
    450                 455                 460

acc act gca gac tca tct ttg ttg caa acc aac att gcg ctg cag ctg  1440
Thr Thr Ala Asp Ser Ser Leu Leu Gln Thr Asn Ile Ala Leu Gln Leu
465                 470                 475                 480

atg gag aaa agc cag aag gaa tat gaa aaa tta gct gcc agt tta aat  1488
Met Glu Lys Ser Gln Lys Glu Tyr Glu Lys Leu Ala Ala Ser Leu Asn
                485                 490                 495

gaa gca aga caa gaa cta agt gac aaa gta aga gaa ctt tcc aga tct  1536
Glu Ala Arg Gln Glu Leu Ser Asp Lys Val Arg Glu Leu Ser Arg Ser
            500                 505                 510

gct ggc aaa aca tcc ctt gtg gag gag gca gaa aag cac gcg cgg tcc  1584
Ala Gly Lys Thr Ser Leu Val Glu Glu Ala Glu Lys His Ala Arg Ser
        515                 520                 525
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tta caa gag ctg gca aag cag ctg gaa gag atc aag aga aac gcc agc   1632
Leu Gln Glu Leu Ala Lys Gln Leu Glu Glu Ile Lys Arg Asn Ala Ser
    530                 535                 540

ggg gat gag ctg gtg cgc tgt gct gtg gat gcc gcc acc gcc tac gag   1680
Gly Asp Glu Leu Val Arg Cys Ala Val Asp Ala Ala Thr Ala Tyr Glu
545                 550                 555                 560

aac atc ctc aat gcc atc aaa gcg gcc gag gac gca gcc aac agg gct   1728
Asn Ile Leu Asn Ala Ile Lys Ala Ala Glu Asp Ala Ala Asn Arg Ala
                565                 570                 575

gcc agt gca tct gaa tct gcc ctc cag aca gtg ata aag gaa gat ctg   1776
Ala Ser Ala Ser Glu Ser Ala Leu Gln Thr Val Ile Lys Glu Asp Leu
            580                 585                 590

cca aga aaa gct aaa acc ctg agt tcc aac agt gat aaa ctg tta aat   1824
Pro Arg Lys Ala Lys Thr Leu Ser Ser Asn Ser Asp Lys Leu Leu Asn
        595                 600                 605

gaa gcc aag atg aca caa aag aag cta aag caa gaa gtc agt cca gct   1872
Glu Ala Lys Met Thr Gln Lys Lys Leu Lys Gln Glu Val Ser Pro Ala
    610                 615                 620

ctc aac aac cta cag caa acc ctg aat att gtg aca gtt cag aaa gaa   1920
Leu Asn Asn Leu Gln Gln Thr Leu Asn Ile Val Thr Val Gln Lys Glu
625                 630                 635                 640

gtg ata gac acc aat ctc aca act ctc cga gat ggt ctt cat ggg ata   1968
Val Ile Asp Thr Asn Leu Thr Thr Leu Arg Asp Gly Leu His Gly Ile
                645                 650                 655

cag aga ggt gat att gat gct atg atc agt agt gca aag agc atg gtc   2016
Gln Arg Gly Asp Ile Asp Ala Met Ile Ser Ser Ala Lys Ser Met Val
            660                 665                 670

aga aag gcc aac gac atc aca gat gag gtt ctg gat ggg ctc aac ccc   2064
Arg Lys Ala Asn Asp Ile Thr Asp Glu Val Leu Asp Gly Leu Asn Pro
        675                 680                 685

atc cag aca gat gtg gaa aga att aag gac acc tat ggg agg aca cag   2112
Ile Gln Thr Asp Val Glu Arg Ile Lys Asp Thr Tyr Gly Arg Thr Gln
    690                 695                 700

aac gaa gac ttc aaa aag gct ctg act gat gca gat aac tcg gtg aat   2160
Asn Glu Asp Phe Lys Lys Ala Leu Thr Asp Ala Asp Asn Ser Val Asn
705                 710                 715                 720

aag tta acc aac aaa cta cct gat ctt tgg cgc aag att gaa agt atc   2208
Lys Leu Thr Asn Lys Leu Pro Asp Leu Trp Arg Lys Ile Glu Ser Ile
                725                 730                 735

aac caa cag ctg ttg ccc ttg gga aac atc tct gac aac atg gac aga   2256
Asn Gln Gln Leu Leu Pro Leu Gly Asn Ile Ser Asp Asn Met Asp Arg
            740                 745                 750

ata cga gaa cta att cag cag gcc aga gat gct gcc agt aag gtt gct   2304
Ile Arg Glu Leu Ile Gln Gln Ala Arg Asp Ala Ala Ser Lys Val Ala
        755                 760                 765

gtc ccc atg agg ttc aat ggt aaa tct gga gtc gaa gtc cga ctg cca   2352
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Val Pro Met Arg Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro
    770                 775                 780

aat gac ctg gaa gat ttg aaa gga tat aca tct ctg tcc ttg ttt ctc   2400
Asn Asp Leu Glu Asp Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu
785                 790                 795                 800

caa agg ccc aac tca aga gaa aat ggg ggt act gag aat atg ttt gtg   2448
Gln Arg Pro Asn Ser Arg Glu Asn Gly Gly Thr Glu Asn Met Phe Val
                805                 810                 815

atg tac ctt gga aat aaa gat gcc tcc cgg gac tac atc ggc atg gca   2496
Met Tyr Leu Gly Asn Lys Asp Ala Ser Arg Asp Tyr Ile Gly Met Ala
            820                 825                 830

gtt gtg gat ggc cag ctc acc tgt gtc tac aac ctg ggg gac cgt gag   2544
Val Val Asp Gly Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu
        835                 840                 845

gct gaa ctc caa gtg gac cag atc ttg acc aag agt gag act aag gag   2592
Ala Glu Leu Gln Val Asp Gln Ile Leu Thr Lys Ser Glu Thr Lys Glu
    850                 855                 860

gca gtt atg gat cgg gtg aaa ttt cag aga att tat cag ttt gca agg   2640
Ala Val Met Asp Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Arg
865                 870                 875                 880

ctt aat tac acc aaa gga gcc aca tcc agt aaa cca gaa aca ccc gga   2688
Leu Asn Tyr Thr Lys Gly Ala Thr Ser Ser Lys Pro Glu Thr Pro Gly
                885                 890                 895

gtc tat gac atg gat ggt aga aat agc aat aca ctc ctt aat ttg gat   2736
Val Tyr Asp Met Asp Gly Arg Asn Ser Asn Thr Leu Leu Asn Leu Asp
            900                 905                 910

cct gaa aat gtt gta ttt tat gtt gga ggt tac cca cct gat ttt aaa   2784
Pro Glu Asn Val Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Lys
        915                 920                 925

ctt ccc agt cga cta agt ttc cct cca tac aaa ggt tgt att gaa tta   2832
Leu Pro Ser Arg Leu Ser Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu
    930                 935                 940

gat gac ctc aat gaa aat gtt ctg agc ttg tac aac ttc aaa aaa aca   2880
Asp Asp Leu Asn Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Lys Thr
945                 950                 955                 960

ttc aat ctc aac aca act gaa gtg gag cct tgt aga agg agg aag gaa   2928
Phe Asn Leu Asn Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu
                965                 970                 975

gag tca gac aaa aat tat ttt gaa ggt acg ggc tat gct cga gtt cca   2976
Glu Ser Asp Lys Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Val Pro
            980                 985                 990

act caa cca cat gct ccc atc cca acc ttt gga cag aca att cag acc   3024
Thr Gln Pro His Ala Pro Ile Pro Thr Phe Gly Gln Thr Ile Gln Thr
        995                1000                1005

acc gtg gat aga ggc ttg ctg ttc ttt gca gaa aac ggg gat cgc ttc   3072
Thr Val Asp Arg Gly Leu Leu Phe Phe Ala Glu Asn Gly Asp Arg Phe
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   1010                1015                1020

ata tct cta aat ata gaa gat ggc aag ctc atg gtg aga tac aaa ctg   3120
Ile Ser Leu Asn Ile Glu Asp Gly Lys Leu Met Val Arg Tyr Lys Leu
1025                1030                1035                1040

aat tca gag cta cca aaa gag aga gga gtt gga gac gcc ata aac aac   3168
Asn Ser Glu Leu Pro Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn
                1045                1050                1055

ggc aga gac cat tcg att cag atc aaa att gga aaa ctc caa aag cgt   3216
Gly Arg Asp His Ser Ile Gln Ile Lys Ile Gly Lys Leu Gln Lys Arg
            1060                1065                1070

atg tgg ata aat gtg gac gtt caa aac act ata att gat ggt gaa gta   3264
Met Trp Ile Asn Val Asp Val Gln Asn Thr Ile Ile Asp Gly Glu Val
        1075                1080                1085

ttt gat ttc agc aca tat tat ctg gga gga att cca att gca atc agg   3312
Phe Asp Phe Ser Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg
    1090                1095                1100

gaa aga ttt aac att tct acg cct gct ttc cga ggc tgc atg aaa aat   3360
Glu Arg Phe Asn Ile Ser Thr Pro Ala Phe Arg Gly Cys Met Lys Asn
1105                1110                1115                1120

ttg aag aaa acc agt ggt gtc gtt aga ttg aat gat act gtg gga gta   3408
Leu Lys Lys Thr Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val
                1125                1130                1135

acc aaa aag tgc tcg gaa gac tgg aag ctt gtg cga tct gcc tca ttc   3456
Thr Lys Lys Cys Ser Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe
            1140                1145                1150

tcc aga gga gga caa ttg agt ttc act gat ttg ggc tta cca cct act   3504
Ser Arg Gly Gly Gln Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr
        1155                1160                1165

gac cac ctc cag gcc tca ttt gga ttt cag acc ttt caa ccc agt ggc   3552
Asp His Leu Gln Ala Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly
    1170                1175                1180

ata tta tta gat cat cag aca tgg aca agg aac ctg cag gtc act ctg   3600
Ile Leu Leu Asp His Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu
1185                1190                1195                1200

gaa gat ggt tac att gaa ttg agc acc agc gat agc ggc ggc cca att   3648
Glu Asp Gly Tyr Ile Glu Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile
                1205                1210                1215

ttt aaa tct cca cag acg tat atg gat ggt tta ctg cat tat gta tct   3696
Phe Lys Ser Pro Gln Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser
            1220                1225                1230

gta ata agc gac aac tct gga cta cgg ctt ctc atc gat gac cag ctt   3744
Val Ile Ser Asp Asn Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu
        1235                1240                1245

ctg aga aat agc aaa agg cta aaa cac att tca agt tcc cgg cag tct   3792
Leu Arg Asn Ser Lys Arg Leu Lys His Ile Ser Ser Ser Arg Gln Ser
    1250                1255                1260
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ctg cgt ctg ggc ggg agc aat ttt gag ggt tgt att agc aat gtt ttt   3840
Leu Arg Leu Gly Gly Ser Asn Phe Glu Gly Cys Ile Ser Asn Val Phe
1265                1270                1275                1280

gtc cag agg tta tca ctg agt cct gaa gtc cta gat ttg acc agt aac   3888
Val Gln Arg Leu Ser Leu Ser Pro Glu Val Leu Asp Leu Thr Ser Asn
                1285                1290                1295

tct ctc aag aga gat gtg tcc ctg gga ggc tgc agt tta aac aaa cca   3936
Ser Leu Lys Arg Asp Val Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro
            1300                1305                1310

cct ttt cta atg ttg ctt aaa ggt tct acc agg ttt aac aag acc aag   3984
Pro Phe Leu Met Leu Leu Lys Gly Ser Thr Arg Phe Asn Lys Thr Lys
        1315                1320                1325

act ttt cgt atc aac cag ctg ttg cag gac aca cca gtg gcc tcc cca   4032
Thr Phe Arg Ile Asn Gln Leu Leu Gln Asp Thr Pro Val Ala Ser Pro
    1330                1335                1340

agg agc gtg aag gtg tgg caa gat gct tgc tca cca ctt ccc aag acc   4080
Arg Ser Val Lys Val Trp Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr
1345                1350                1355                1360

cag gcc aat cat gga gcc ctc cag ttt ggg gac att ccc acc agc cac   4128
Gln Ala Asn His Gly Ala Leu Gln Phe Gly Asp Ile Pro Thr Ser His
                1365                1370                1375

ttg cta ttc aag ctt cct cag gag ctg ctg aaa ccc agg tca cag ttt   4176
Leu Leu Phe Lys Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe
            1380                1385                1390

gct gtg gac atg cag aca aca tcc tcc aga gga ctg gtg ttt cac acg   4224
Ala Val Asp Met Gln Thr Thr Ser Ser Arg Gly Leu Val Phe His Thr
        1395                1400                1405

ggc act aag aac tcc ttt atg gct ctt tat ctt tca aaa gga cgt ctg   4272
Gly Thr Lys Asn Ser Phe Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu
    1410                1415                1420

gtc ttt gca ctg ggg aca gat ggg aaa aaa ttg agg atc aaa agc aag   4320
Val Phe Ala Leu Gly Thr Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys
1425                1430                1435                1440

gag aaa tgc aat gat ggg aaa tgg cac acg gtg gtg ttt ggc cat gat   4368
Glu Lys Cys Asn Asp Gly Lys Trp His Thr Val Val Phe Gly His Asp
                1445                1450                1455

ggg gaa aag ggg cgc ttg gtt gtg gat gga ctg agg gcc cgg gag gga   4416
Gly Glu Lys Gly Arg Leu Val Val Asp Gly Leu Arg Ala Arg Glu Gly
            1460                1465                1470

agt ttg cct gga aac tcc acc atc agc atc aga gcg cca gtt tac ctg   4464
Ser Leu Pro Gly Asn Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu
        1475                1480                1485

gga tca cct cca tca ggg aaa cca aag agc ctc ccc aca aac agc ttt   4512
Gly S r Pro Pro Ser Gly Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe
    1490                1495                1500
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gtg gga tgc ctg aag aac ttt cag ctg gat tca aaa ccc ttg tat acc   4560
Val Gly Cys Leu Lys Asn Phe Gln Leu Asp Ser Lys Pro Leu Tyr Thr
1505                1510                1515                1520

cct tct tca agc ttc ggg gtg tct tcc tgc ttg ggt ggt cct ttg gag   4608
Pro Ser Ser Ser Phe Gly Val Ser Ser Cys Leu Gly Gly Pro Leu Glu
                1525                1530                1535

aaa ggc att tat ttc tct gaa gaa gga ggt cat gtc gtc ttg gct cac   4656
Lys Gly Ile Tyr Phe Ser Glu Glu Gly Gly His Val Val Leu Ala His
            1540                1545                1550

tct gta ttg ttg ggg cca gaa ttt aag ctt gtt ttc agc atc cgc cca   4704
Ser Val Leu Leu Gly Pro Glu Phe Lys Leu Val Phe Ser Ile Arg Pro
        1555                1560                1565

aga agt ctc act ggg atc cta ata cac atc gga agt cag ccc ggg aag   4752
Arg Ser Leu Thr Gly Ile Leu Ile His Ile Gly Ser Gln Pro Gly Lys
    1570                1575                1580

cac tta tgt gtt tac ctg gag gca gga aag gtc acg gcc tct atg gac   4800
His Leu Cys Val Tyr Leu Glu Ala Gly Lys Val Thr Ala Ser Met Asp
1585                1590                1595                1600

agt ggg gca ggt ggg acc tca acg tcg gtc aca cca aag cag tct ctg   4848
Ser Gly Ala Gly Gly Thr Ser Thr Ser Val Thr Pro Lys Gln Ser Leu
                1605                1610                1615

tgt gat gga cag tgg cac tcg gtg gca gtc acc ata aaa caa cac atc   4896
Cys Asp Gly Gln Trp His Ser Val Ala Val Thr Ile Lys Gln His Ile
            1620                1625                1630

ctg cac ctg gaa ctg gac aca gac agt agc tac aca gct gga cag atc   4944
Leu His Leu Glu Leu Asp Thr Asp Ser Ser Tyr Thr Ala Gly Gln Ile
        1635                1640                1645

ccc ttc cca cct gcc agc act caa gag cca cta cac ctt gga ggt gct   4992
Pro Phe Pro Pro Ala Ser Thr Gln Glu Pro Leu His Leu Gly Gly Ala
    1650                1655                1660

cca gcc aat ttg acg aca ctg agg atc cct gtg tgg aaa tca ttc ttt   5040
Pro Ala Asn Leu Thr Thr Leu Arg Ile Pro Val Trp Lys Ser Phe Phe
1665                1670                1675                1680

ggc tgt ctg agg aat att cat gtc aat cac atc cct gtc cct gtc act   5088
Gly Cys Leu Arg Asn Ile His Val Asn His Ile Pro Val Pro Val Thr
                1685                1690                1695

gaa gcc ttg gaa gtc cag ggg cct gtc agt ctg aat ggt tgt cct gac   5136
Glu Ala Leu Glu Val Gln Gly Pro Val Ser Leu Asn Gly Cys Pro Asp
            1700                1705                1710

cag taacccaagc ctatttcaca gcaaggaaat tcaccttcaa aagcactgat        5189
Gln

tacccaatgc acctccctcc ccagctcgag atcattcttc aattaggaca caaaccagac 5249

aggtttaata gcgaatctaa ttttgaattc tgaccatgga tacccatcac tttggcattc 5309

agtgctacat gtgtatttta tataaaaatc ccatttcttg aagataaaaa aattgttatt 5369
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caaattgtta tgcacagaat gtttttggta atattaattt ccactaaaaa attaaatgtc 5429

tttt 5433

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<212> PRT
<213> Homo sapiens

<400> 6

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Met Gly Trp Leu Trp Ile Phe Gly Ala Ala Leu Gly Gln Cys Leu Gly
  1               5                  10                  15

Tyr Ser Ser Gln Gln Gln Arg Val Pro Phe Leu Gln Pro Pro Gly Gln
             20                  25                  30

Ser Gln Leu Gln Ala Ser Tyr Val Glu Phe Arg Pro Ser Gln Gly Cys
         35                  40                  45

Ser Pro Gly Tyr Tyr Arg Asp His Lys Gly Leu Tyr Thr Gly Arg Cys
     50                  55                  60

Val Pro Cys Asn Cys Asn Gly His Ser Asn Gln Cys Gln Asp Gly Ser
 65                  70                  75                  80

Gly Ile Cys Val Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu
                 85                  90                  95

Arg Cys Gln Glu Gly Tyr Tyr Gly Asn Ala Val His Gly Ser Cys Arg
            100                 105                 110

Ala Cys Pro Cys Pro His Thr Asn Ser Phe Ala Thr Gly Cys Val Val
        115                 120                 125

Asn Gly Gly Asp Val Arg Cys Ser Cys Lys Ala Gly Tyr Thr Gly Thr
    130                 135                 140

Gln Cys Glu Arg Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe
145                 150                 155                 160

Gly Gly Ser Cys Gln Pro Cys Ser Cys Asn Ser Asn Gly Gln Leu Gly
                165                 170                 175

Ser Cys His Pro Leu Thr Gly Asp Cys Ile Asn Gln Glu Pro Lys Asp
            180                 185                 190

Ser Ser Pro Ala Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr
        195                 200                 205

Leu Leu Asn Asp Leu Ala Thr Met Gly Glu Gln Leu Arg Leu Val Lys
    210                 215                 220

Ser Gln Leu Gln Gly Leu Ser Ala Ser Ala Gly Leu Leu Glu Gln Met
225                 230                 235                 240

Arg His Met Glu Thr Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Asn
                245                 250                 255

Tyr Arg Ser Ala Ile Ser Asn His Gly Ser Lys Ile Glu Gly Leu Glu
            260                 265                 270
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Arg Glu Leu Thr Asp Leu Asn Gln Glu Phe Glu Thr Leu Gln Glu Lys
        275                 280                 285

Ala Gln Val Asn Ser Arg Lys Ala Gln Thr Leu Asn Asn Asn Val Asn
    290                 295                 300

Arg Ala Thr Gln Ser Ala Lys Glu Leu Asp Val Lys Ile Lys Asn Val
305                 310                 315                 320

Ile Arg Asn Val His Ile Leu Leu Lys Gln Ile Ser Gly Thr Asp Gly
                325                 330                 335

Glu Gly Asn Asn Val Pro Ser Gly Asp Phe Ser Arg Glu Trp Ala Glu
            340                 345                 350

Ala Gln Arg Met Met Arg Glu Leu Arg Asn Arg Asn Phe Gly Lys His
        355                 360                 365

Leu Arg Glu Ala Glu Ala Asp Lys Arg Glu Ser Gln Leu Leu Leu Asn
    370                 375                 380

Arg Ile Arg Thr Trp Gln Lys Thr His Gln Gly Glu Asn Asn Gly Leu
385                 390                 395                 400

Ala Asn Ser Ile Arg Asp Ser Leu Asn Glu Tyr Glu Ala Lys Leu Ser
                405                 410                 415

Asp Leu Arg Ala Arg Leu Gln Glu Ala Ala Ala Gln Ala Lys Gln Ala
            420                 425                 430

Asn Gly Leu Asn Gln Glu Asn Glu Arg Ala Leu Gly Ala Ile Gln Arg
        435                 440                 445

Gln Val Lys Glu Ile Asn Ser Leu Gln Ser Asp Phe Thr Lys Tyr Leu
    450                 455                 460

Thr Thr Ala Asp Ser Ser Leu Leu Gln Thr Asn Ile Ala Leu Gln Leu
465                 470                 475                 480

Met Glu Lys Ser Gln Lys Glu Tyr Glu Lys Leu Ala Ala Ser Leu Asn
                485                 490                 495

Glu Ala Arg Gln Glu Leu Ser Asp Lys Val Arg Glu Leu Ser Arg Ser
            500                 505                 510

Ala Gly Lys Thr Ser Leu Val Glu Glu Ala Glu Lys His Ala Arg Ser
        515                 520                 525

Leu Gln Glu Leu Ala Lys Gln Leu Glu Glu Ile Lys Arg Asn Ala Ser
    530                 535                 540

Gly Asp Glu Leu Val Arg Cys Ala Val Asp Ala Ala Thr Ala Tyr Glu
545                 550                 555                 560

Asn Ile Leu Asn Ala Ile Lys Ala Ala Glu Asp Ala Ala Asn Arg Ala
                565                 570                 575

Ala Ser Ala Ser Glu Ser Ala L u Gln Thr Val Ile Lys Glu Asp Leu
            580                 585                 590
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Pro Arg Lys Ala Lys Thr Leu Ser Ser Asn Ser Asp Lys Leu Leu Asn
595 600 605

Glu Ala Lys Met Thr Gln Lys Lys Leu Lys Gln Glu Val Ser Pro Ala
610 615 620

Leu Asn Asn Leu Gln Gln Thr Leu Asn Ile Val Thr Val Gln Lys Glu
625 630 635 640

Val Ile Asp Thr Asn Leu Thr Thr Leu Arg Asp Gly Leu His Gly Ile
645 650 655

Gln Arg Gly Asp Ile Asp Ala Met Ile Ser Ser Ala Lys Ser Met Val
660 665 670

Arg Lys Ala Asn Asp Ile Thr Asp Glu Val Leu Asp Gly Leu Asn Pro
675 680 685

Ile Gln Thr Asp Val Glu Arg Ile Lys Asp Thr Tyr Gly Arg Thr Gln
690 695 700

Asn Glu Asp Phe Lys Lys Ala Leu Thr Asp Ala Asp Asn Ser Val Asn
705 710 715 720

Lys Leu Thr Asn Lys Leu Pro Asp Leu Trp Arg Lys Ile Glu Ser Ile
725 730 735

Asn Gln Gln Leu Leu Pro Leu Gly Asn Ile Ser Asp Asn Met Asp Arg
740 745 750

Ile Arg Glu Leu Ile Gln Gln Ala Arg Asp Ala Ala Ser Lys Val Ala
755 760 765

Val Pro Met Arg Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro
770 775 780

Asn Asp Leu Glu Asp Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu
785 790 795 800

Gln Arg Pro Asn Ser Arg Glu Asn Gly Gly Thr Glu Asn Met Phe Val
805 810 815

Met Tyr Leu Gly Asn Lys Asp Ala Ser Arg Asp Tyr Ile Gly Met Ala
820 825 830

Val Val Asp Gly Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu
835 840 845

Ala Glu Leu Gln Val Asp Gln Ile Leu Thr Lys Ser Glu Thr Lys Glu
850 855 860

Ala Val Met Asp Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Arg
865 870 875 880

Leu Asn Tyr Thr Lys Gly Ala Thr Ser Ser Lys Pro Glu Thr Pro Gly
885 890 895

Val Tyr Asp Met Asp Gly Arg Asn Ser Asn Thr Leu Leu Asn Leu Asp
900 905 910

Pro Glu Asn Val Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Lys

915 920 925

Leu Pro Ser Arg Leu Ser Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu
930 935 940

Asp Asp Leu Asn Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Lys Thr
945 950 955 960

Phe Asn Leu Asn Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu
965 970 975

Glu Ser Asp Lys Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Val Pro
980 985 990

Thr Gln Pro His Ala Pro Ile Pro Thr Phe Gly Gln Thr Ile Gln Thr
995 1000 1005

Thr Val Asp Arg Gly Leu Leu Phe Phe Ala Glu Asn Gly Asp Arg Phe
1010 1015 1020

Ile Ser Leu Asn Ile Glu Asp Gly Lys Leu Met Val Arg Tyr Lys Leu
1025 1030 1035 1040

Asn Ser Glu Leu Pro Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn
1045 1050 1055

Gly Arg Asp His Ser Ile Gln Ile Lys Ile Gly Lys Leu Gln Lys Arg
1060 1065 1070

Met Trp Ile Asn Val Asp Val Gln Asn Thr Ile Ile Asp Gly Glu Val
1075 1080 1085

Phe Asp Phe Ser Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg
1090 1095 1100

Glu Arg Phe Asn Ile Ser Thr Pro Ala Phe Arg Gly Cys Met Lys Asn
1105 1110 1115 1120

Leu Lys Lys Thr Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val
1125 1130 1135

Thr Lys Lys Cys Ser Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe
1140 1145 1150

Ser Arg Gly Gly Gln Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr
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Asp His Leu Gln Ala Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly
1170 1175 1180

Ile Leu Leu Asp His Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu
1185 1190 1195 1200

Glu Asp Gly Tyr Ile Glu Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile
1205 1210 1215

Phe Lys Ser Pro Gln Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser
1220 1225 1230

Val Ile Ser Asp Asn Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu
1235 1240 1245

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Leu Arg Asn Ser Lys Arg Leu Lys His Ile Ser Ser Ser Arg Gln Ser
   1250                1255                1260

Leu Arg Leu Gly Gly Ser Asn Phe Glu Gly Cys Ile Ser Asn Val Phe
1265                1270                1275                1280

Val Gln Arg Leu Ser Leu Ser Pro Glu Val Leu Asp Leu Thr Ser Asn
                1285                1290                1295

Ser Leu Lys Arg Asp Val Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro
            1300                1305                1310

Pro Phe Leu Met Leu Leu Lys Gly Ser Thr Arg Phe Asn Lys Thr Lys
        1315                1320                1325

Thr Phe Arg Ile Asn Gln Leu Leu Gln Asp Thr Pro Val Ala Ser Pro
    1330                1335                1340

Arg Ser Val Lys Val Trp Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr
1345                1350                1355                1360

Gln Ala Asn His Gly Ala Leu Gln Phe Gly Asp Ile Pro Thr Ser His
                1365                1370                1375

Leu Leu Phe Lys Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe
            1380                1385                1390

Ala Val Asp Met Gln Thr Thr Ser Ser Arg Gly Leu Val Phe His Thr
        1395                1400                1405

Gly Thr Lys Asn Ser Phe Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu
    1410                1415                1420

Val Phe Ala Leu Gly Thr Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys
1425                1430                1435                1440

Glu Lys Cys Asn Asp Gly Lys Trp His Thr Val Val Phe Gly His Asp
                1445                1450                1455

Gly Glu Lys Gly Arg Leu Val Val Asp Gly Leu Arg Ala Arg Glu Gly
            1460                1465                1470

Ser Leu Pro Gly Asn Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu
        1475                1480                1485

Gly Ser Pro Pro Ser Gly Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe
    1490                1495                1500

Val Gly Cys Leu Lys Asn Phe Gln Leu Asp Ser Lys Pro Leu Tyr Thr
1505                1510                1515                1520

Pro Ser Ser Ser Phe Gly Val Ser Ser Cys Leu Gly Gly Pro Leu Glu
                1525                1530                1535

Lys Gly Ile Tyr Phe Ser Glu Glu Gly Gly His Val Val Leu Ala His
            1540                1545                1550

Ser Val Leu Leu Gly Pro Glu Phe Lys Leu Val Phe Ser Ile Arg Pro
        1555                1560                1565
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Arg Ser Leu Thr Gly Ile Leu Ile His Ile Gly Ser Gln Pro Gly Lys
   1570                1575                1580

His Leu Cys Val Tyr Leu Glu Ala Gly Lys Val Thr Ala Ser Met Asp
1585                1590                1595                1600

Ser Gly Ala Gly Gly Thr Ser Thr Ser Val Thr Pro Lys Gln Ser Leu
               1605                1610                1615

Cys Asp Gly Gln Trp His Ser Val Ala Val Thr Ile Lys Gln His Ile
           1620                1625                1630

Leu His Leu Glu Leu Asp Thr Asp Ser Ser Tyr Thr Ala Gly Gln Ile
       1635                1640                1645

Pro Phe Pro Pro Ala Ser Thr Gln Glu Pro Leu His Leu Gly Gly Ala
   1650                1655                1660

Pro Ala Asn Leu Thr Thr Leu Arg Ile Pro Val Trp Lys Ser Phe Phe
1665                1670                1675                1680

Gly Cys Leu Arg Asn Ile His Val Asn His Ile Pro Val Pro Val Thr
               1685                1690                1695

Glu Ala Leu Glu Val Gln Gly Pro Val Ser Leu Asn Gly Cys Pro Asp
           1700                1705                1710

Gln
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Gln Gln Arg Val Pro Phe Leu Gln Pro Pro Gly Gln Ser Gln Leu Gln
  1               5                  10                  15

gcg agt tat gtg gag ttt aga ccc agc cag ggt tgt agc cct gga tac   96
Ala Ser Tyr Val Glu Phe Arg Pro Ser Gln Gly Cys Ser Pro Gly Tyr
             20                  25                  30

tat cgg gat cat aaa ggc ttg tat acc gga cgg tgt gtt ccc tgc aat   144
Tyr Arg Asp His Lys Gly Leu Tyr Thr Gly Arg Cys Val Pro Cys Asn
         35                  40                  45

tgc aac gga cat tca aat caa tgc cag gat ggc tca ggc ata tgt gtt   192
Cys Asn Gly His Ser Asn Gln Cys Gln Asp Gly Ser Gly Ile Cys Val
     50                  55                  60

aac tgt cag cac aac acc gcg gga gag cac tgt gaa cgc tgc cag gag   240
Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Gln Glu
 65                  70                  75                  80
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ggc tac tat ggc aac gcc gtc cac gga tcc tgc agg gcc tgc cca tgt   288
Gly Tyr Tyr Gly Asn Ala Val His Gly Ser Cys Arg Ala Cys Pro Cys
                85                  90                  95

cct cac act aac agc ttt gcc act ggc tgt gtg gtg aat ggg gga gac   336
Pro His Thr Asn Ser Phe Ala Thr Gly Cys Val Val Asn Gly Gly Asp
            100                 105                 110

gtg cgg tgc tcc tgc aaa gct ggg tac aca gga aca cag tgt gaa agg   384
Val Arg Cys Ser Cys Lys Ala Gly Tyr Thr Gly Thr Gln Cys Glu Arg
        115                 120                 125

tgt gca ccg gga tat ttc ggg aat ccc cag aaa ttc gga ggt agc tgc   432
Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys
    130                 135                 140

caa cca tgc agt tgt aac agc aat ggc cag ctg ggc agc tgt cat ccc   480
Gln Pro Cys Ser Cys Asn Ser Asn Gly Gln Leu Gly Ser Cys His Pro
145                 150                 155                 160

ctg act gga gac tgc ata aac caa gaa ccc aaa gat agc agc cct gca   528
Leu Thr Gly Asp Cys Ile Asn Gln Glu Pro Lys Asp Ser Ser Pro Ala
                165                 170                 175

gaa gaa tgt gat gat tgc gac agc tgt gtg atg acc ctc ctg aac gac   576
Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp
            180                 185                 190

ctg gcc acc atg ggc gag cag ctc cgc ctg gtc aag tct cag ctg cag   624
Leu Ala Thr Met Gly Glu Gln Leu Arg Leu Val Lys Ser Gln Leu Gln
        195                 200                 205

ggc ctg agt gcc agc gca ggg ctt ctg gag cag atg agg cac atg gag   672
Gly Leu Ser Ala Ser Ala Gly Leu Leu Glu Gln Met Arg His Met Glu
    210                 215                 220

acc cag gcc aag gac ctg agg aat cag ttg ctc aac tac cgt tct gcc   720
Thr Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Asn Tyr Arg Ser Ala
225                 230                 235                 240

att tca aat cat gga tca aaa ata gaa ggc ctg gaa aga gaa ctg act   768
Ile Ser Asn His Gly Ser Lys Ile Glu Gly Leu Glu Arg Glu Leu Thr
                245                 250                 255

gat ttg aat caa gaa ttt gag act ttg caa gaa aag gct caa gta aat   816
Asp Leu Asn Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn
            260                 265                 270

tcc aga aaa gca caa aca tta aac aac aat gtt aat cgg gca aca caa   864
Ser Arg Lys Ala Gln Thr Leu Asn Asn Asn Val Asn Arg Ala Thr Gln
        275                 280                 285

agc gca aaa gaa ctg gat gtg aag att aaa aat gtc atc cgg aat gtg   912
Ser Ala Lys Glu Leu Asp Val Lys Ile Lys Asn Val Ile Arg Asn Val
    290                 295                 300

cac att ctt tta aag cag atc tct ggg aca gat gga gag gga aac aac   960
His Ile Leu Leu Lys Gln Ile Ser Gly Thr Asp Gly Glu Gly Asn Asn
305                 310                 315                 320

gtg cct tca ggt gac ttt tcc aga gag tgg gct gaa gcc cag cgc atg   1008
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Val Pro Ser Gly Asp Phe Ser Arg Glu Trp Ala Glu Ala Gln Arg Met
                325                 330                 335

atg agg gaa ctg cgg aac agg aac ttt gga aag cac ctc aga gaa gca   1056
Met Arg Glu Leu Arg Asn Arg Asn Phe Gly Lys His Leu Arg Glu Ala
            340                 345                 350

gaa gct gat aaa agg gag tcg cag ctc ttg ctg aac cgg ata agg acc   1104
Glu Ala Asp Lys Arg Glu Ser Gln Leu Leu Leu Asn Arg Ile Arg Thr
        355                 360                 365

tgg cag aaa acc cac cag ggg gag aac aat ggg ctt gct aac agt atc   1152
Trp Gln Lys Thr His Gln Gly Glu Asn Asn Gly Leu Ala Asn Ser Ile
    370                 375                 380

cgg gat tct tta aat gaa tac gaa gcc aaa ctc agt gac ctt cgt gct   1200
Arg Asp Ser Leu Asn Glu Tyr Glu Ala Lys Leu Ser Asp Leu Arg Ala
385                 390                 395                 400

cgg ctg cag gag gca gct gcc caa gcc aag cag gca aat ggc ttg aac   1248
Arg Leu Gln Glu Ala Ala Ala Gln Ala Lys Gln Ala Asn Gly Leu Asn
                405                 410                 415

caa gaa aac gag aga gct ttg gga gcc att cag aga caa gtg aaa gaa   1296
Gln Glu Asn Glu Arg Ala Leu Gly Ala Ile Gln Arg Gln Val Lys Glu
            420                 425                 430

ata aat tcc ctg cag agt gat ttc acc aag tat cta acc act gca gac   1344
Ile Asn Ser Leu Gln Ser Asp Phe Thr Lys Tyr Leu Thr Thr Ala Asp
        435                 440                 445

tca tct ttg ttg caa acc aac att gcg ctg cag ctg atg gag aaa agc   1392
Ser Ser Leu Leu Gln Thr Asn Ile Ala Leu Gln Leu Met Glu Lys Ser
    450                 455                 460

cag aag gaa tat gaa aaa tta gct gcc agt tta aat gaa gca aga caa   1440
Gln Lys Glu Tyr Glu Lys Leu Ala Ala Ser Leu Asn Glu Ala Arg Gln
465                 470                 475                 480

gaa cta agt gac aaa gta aga gaa ctt tcc aga tct gct ggc aaa aca   1488
Glu Leu Ser Asp Lys Val Arg Glu Leu Ser Arg Ser Ala Gly Lys Thr
                485                 490                 495

tcc ctt gtg gag gag gca gaa aag cac gcg cgg tcc tta caa gag ctg   1536
Ser Leu Val Glu Glu Ala Glu Lys His Ala Arg Ser Leu Gln Glu Leu
            500                 505                 510

gca aag cag ctg gaa gag atc aag aga aac gcc agc ggg gat gag ctg   1584
Ala Lys Gln Leu Glu Glu Ile Lys Arg Asn Ala Ser Gly Asp Glu Leu
        515                 520                 525

gtg cgc tgt gct gtg gat gcc gcc acc gcc tac gag aac atc ctc aat   1632
Val Arg Cys Ala Val Asp Ala Ala Thr Ala Tyr Glu Asn Ile Leu Asn
    530                 535                 540

gcc atc aaa gcg gcc gag gac gca gcc aac agg gct gcc agt gca tct   1680
Ala Ile Lys Ala Ala Glu Asp Ala Ala Asn Arg Ala Ala Ser Ala Ser
545                 550                 555                 560

gaa tct gcc ctc cag aca gtg ata aag gaa gat ctg cca aga aaa gct   1728
Glu Ser Ala Leu Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Lys Ala
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                565                 570                 575

aaa acc ctg agt tcc aac agt gat aaa ctg tta aat gaa gcc aag atg   1776
Lys Thr Leu Ser Ser Asn Ser Asp Lys Leu Leu Asn Glu Ala Lys Met
            580                 585                 590

aca caa aag aag cta aag caa gaa gtc agt cca gct ctc aac aac cta   1824
Thr Gln Lys Lys Leu Lys Gln Glu Val Ser Pro Ala Leu Asn Asn Leu
        595                 600                 605

cag caa acc ctg aat att gtg aca gtt cag aaa gaa gtg ata gac acc   1872
Gln Gln Thr Leu Asn Ile Val Thr Val Gln Lys Glu Val Ile Asp Thr
    610                 615                 620

aat ctc aca act ctc cga gat ggt ctt cat ggg ata cag aga ggt gat   1920
Asn Leu Thr Thr Leu Arg Asp Gly Leu His Gly Ile Gln Arg Gly Asp
625                 630                 635                 640

att gat gct atg atc agt agt gca aag agc atg gtc aga aag gcc aac   1968
Ile Asp Ala Met Ile Ser Ser Ala Lys Ser Met Val Arg Lys Ala Asn
                645                 650                 655

gac atc aca gat gag gtt ctg gat ggg ctc aac ccc atc cag aca gat   2016
Asp Ile Thr Asp Glu Val Leu Asp Gly Leu Asn Pro Ile Gln Thr Asp
            660                 665                 670

gtg gaa aga att aag gac acc tat ggg agg aca cag aac gaa gac ttc   2064
Val Glu Arg Ile Lys Asp Thr Tyr Gly Arg Thr Gln Asn Glu Asp Phe
        675                 680                 685

aaa aag gct ctg act gat gca gat aac tcg gtg aat aag tta acc aac   2112
Lys Lys Ala Leu Thr Asp Ala Asp Asn Ser Val Asn Lys Leu Thr Asn
    690                 695                 700

aaa cta cct gat ctt tgg cgc aag att gaa agt atc aac caa cag ctg   2160
Lys Leu Pro Asp Leu Trp Arg Lys Ile Glu Ser Ile Asn Gln Gln Leu
705                 710                 715                 720

ttg ccc ttg gga aac atc tct gac aac atg gac aga ata cga gaa cta   2208
Leu Pro Leu Gly Asn Ile Ser Asp Asn Met Asp Arg Ile Arg Glu Leu
                725                 730                 735

att cag cag gcc aga gat gct gcc agt aag gtt gct gtc ccc atg agg   2256
Ile Gln Gln Ala Arg Asp Ala Ala Ser Lys Val Ala Val Pro Met Arg
            740                 745                 750

ttc aat ggt aaa tct gga gtc gaa gtc cga ctg cca aat gac ctg gaa   2304
Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu
        755                 760                 765

gat ttg aaa gga tat aca tct ctg tcc ttg ttt ctc caa agg ccc aac   2352
Asp Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asn
    770                 775                 780

tca aga gaa aat ggg ggt act gag aat atg ttt gtg atg tac ctt gga   2400
Ser Arg Glu Asn Gly Gly Thr Glu Asn Met Phe Val Met Tyr Leu Gly
785                 790                 795                 800

aat aaa gat gcc tcc cgg gac tac atc ggc atg gca gtt gtg gat ggc   2448
Asn Lys Asp Ala Ser Arg Asp Tyr Ile Gly Met Ala Val Val Asp Gly
                805                 810                 815
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cag ctc acc tgt gtc tac aac ctg ggg gac cgt gag gct gaa ctc caa   2496
Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Leu Gln
            820                 825                 830

gtg gac cag atc ttg acc aag agt gag act aag gag gca gtt atg gat   2544
Val Asp Gln Ile Leu Thr Lys Ser Glu Thr Lys Glu Ala Val Met Asp
        835                 840                 845

cgg gtg aaa ttt cag aga att tat cag ttt gca agg ctt aat tac acc   2592
Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Arg Leu Asn Tyr Thr
    850                 855                 860

aaa gga gcc aca tcc agt aaa cca gaa aca ccc gga gtc tat gac atg   2640
Lys Gly Ala Thr Ser Ser Lys Pro Glu Thr Pro Gly Val Tyr Asp Met
865                 870                 875                 880

gat ggt aga aat agc aat aca ctc ctt aat ttg gat cct gaa aat gtt   2688
Asp Gly Arg Asn Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asn Val
                885                 890                 895

gta ttt tat gtt gga ggt tac cca cct gat ttt aaa ctt ccc agt cga   2736
Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Lys Leu Pro Ser Arg
            900                 905                 910

cta agt ttc cct cca tac aaa ggt tgt att gaa tta gat gac ctc aat   2784
Leu Ser Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn
        915                 920                 925

gaa aat gtt ctg agc ttg tac aac ttc aaa aaa aca ttc aat ctc aac   2832
Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Lys Thr Phe Asn Leu Asn
    930                 935                 940

aca act gaa gtg gag cct tgt aga agg agg aag gaa gag tca gac aaa   2880
Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys
945                 950                 955                 960

aat tat ttt gaa ggt acg ggc tat gct cga gtt cca act caa cca cat   2928
Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Val Pro Thr Gln Pro His
                965                 970                 975

gct ccc atc cca acc ttt gga cag aca att cag acc acc gtg gat aga   2976
Ala Pro Ile Pro Thr Phe Gly Gln Thr Ile Gln Thr Thr Val Asp Arg
            980                 985                 990

ggc ttg ctg ttc ttt gca gaa aac ggg gat cgc ttc ata tct cta aat   3024
Gly Leu Leu Phe Phe Ala Glu Asn Gly Asp Arg Phe Ile Ser Leu Asn
        995                1000                1005

ata gaa gat ggc aag ctc atg gtg aga tac aaa ctg aat tca gag cta   3072
Ile Glu Asp Gly Lys Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Leu
   1010                1015                1020

cca aaa gag aga gga gtt gga gac gcc ata aac aac ggc aga gac cat   3120
Pro Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn Gly Arg Asp His
1025                1030                1035                1040

tcg att cag atc aaa att gga aaa ctc caa aag cgt atg tgg ata aat   3168
Ser Ile Gln Ile Lys Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn
                1045                1050                1055
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gtg gac gtt caa aac act ata att gat ggt gaa gta ttt gat ttc agc   3216
Val Asp Val Gln Asn Thr Ile Ile Asp Gly Glu Val Phe Asp Phe Ser
          1060                1065                1070

aca tat tat ctg gga gga att cca att gca atc agg gaa aga ttt aac   3264
Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn
      1075                1080                1085

att tct acg cct gct ttc cga ggc tgc atg aaa aat ttg aag aaa acc   3312
Ile Ser Thr Pro Ala Phe Arg Gly Cys Met Lys Asn Leu Lys Lys Thr
  1090                1095                1100

agt ggt gtc gtt aga ttg aat gat act gtg gga gta acc aaa aag tgc   3360
Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys
1105                1110                1115                1120

tcg gaa gac tgg aag ctt gtg cga tct gcc tca ttc tcc aga gga gga   3408
Ser Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe Ser Arg Gly Gly
              1125                1130                1135

caa ttg agt ttc act gat ttg ggc tta cca cct act gac cac ctc cag   3456
Gln Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr Asp His Leu Gln
          1140                1145                1150

gcc tca ttt gga ttt cag acc ttt caa ccc agt ggc ata tta tta gat   3504
Ala Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Ile Leu Leu Asp
      1155                1160                1165

cat cag aca tgg aca agg aac ctg cag gtc act ctg gaa gat ggt tac   3552
His Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu Glu Asp Gly Tyr
  1170                1175                1180

att gaa ttg agc acc agc gat agc ggc ggc cca att ttt aaa tct cca   3600
Ile Glu Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile Phe Lys Ser Pro
1185                1190                1195                1200

cag acg tat atg gat ggt tta ctg cat tat gta tct gta ata agc gac   3648
Gln Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser Val Ile Ser Asp
              1205                1210                1215

aac tct gga cta cgg ctt ctc atc gat gac cag ctt ctg aga aat agc   3696
Asn Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu Leu Arg Asn Ser
          1220                1225                1230

aaa agg cta aaa cac att tca agt tcc cgg cag tct ctg cgt ctg ggc   3744
Lys Arg Leu Lys His Ile Ser Ser Ser Arg Gln Ser Leu Arg Leu Gly
      1235                1240                1245

ggg agc aat ttt gag ggt tgt att agc aat gtt ttt gtc cag agg tta   3792
Gly Ser Asn Phe Glu Gly Cys Ile Ser Asn Val Phe Val Gln Arg Leu
  1250                1255                1260

tca ctg agt cct gaa gtc cta gat ttg acc agt aac tct ctc aag aga   3840
Ser Leu Ser Pro Glu Val Leu Asp Leu Thr Ser Asn Ser Leu Lys Arg
1265                1270                1275                1280

gat gtg tcc ctg gga ggc tgc agt tta aac aaa cca cct ttt cta atg   3888
Asp Val Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met
              1285                1290                1295

ttg ctt aaa ggt tct acc agg ttt aac aag acc aag act ttt cgt atc   3936
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Leu Leu Lys Gly Ser Thr Arg Phe Asn Lys Thr Lys Thr Phe Arg Ile
          1300                1305                1310

aac cag ctg ttg cag gac aca cca gtg gcc tcc cca agg agc gtg aag   3984
Asn Gln Leu Leu Gln Asp Thr Pro Val Ala Ser Pro Arg Ser Val Lys
       1315                1320                1325

gtg tgg caa gat gct tgc tca cca ctt ccc aag acc cag gcc aat cat   4032
Val Trp Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr Gln Ala Asn His
   1330                1335                1340

gga gcc ctc cag ttt ggg gac att ccc acc agc cac ttg cta ttc aag   4080
Gly Ala Leu Gln Phe Gly Asp Ile Pro Thr Ser His Leu Leu Phe Lys
1345                1350                1355                1360

ctt cct cag gag ctg ctg aaa ccc agg tca cag ttt gct gtg gac atg   4128
Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ala Val Asp Met
               1365                1370                1375

cag aca aca tcc tcc aga gga ctg gtg ttt cac acg ggc act aag aac   4176
Gln Thr Thr Ser Ser Arg Gly Leu Val Phe His Thr Gly Thr Lys Asn
          1380                1385                1390

tcc ttt atg gct ctt tat ctt tca aaa gga cgt ctg gtc ttt gca ctg   4224
Ser Phe Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu Val Phe Ala Leu
       1395                1400                1405

ggg aca gat ggg aaa aaa ttg agg atc aaa agc aag gag aaa tgc aat   4272
Gly Thr Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys Glu Lys Cys Asn
   1410                1415                1420

gat ggg aaa tgg cac acg gtg gtg ttt ggc cat gat ggg gaa aag ggg   4320
Asp Gly Lys Trp His Thr Val Val Phe Gly His Asp Gly Glu Lys Gly
1425                1430                1435                1440

cgc ttg gtt gtg gat gga ctg agg gcc cgg gag gga agt ttg cct gga   4368
Arg Leu Val Val Asp Gly Leu Arg Ala Arg Glu Gly Ser Leu Pro Gly
               1445                1450                1455

aac tcc acc atc agc atc aga gcg cca gtt tac ctg gga tca cct cca   4416
Asn Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu Gly Ser Pro Pro
          1460                1465                1470

tca ggg aaa cca aag agc ctc ccc aca aac agc ttt gtg gga tgc ctg   4464
Ser Gly Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe Val Gly Cys Leu
       1475                1480                1485

aag aac ttt cag ctg gat tca aaa ccc ttg tat acc cct tct tca agc   4512
Lys Asn Phe Gln Leu Asp Ser Lys Pro Leu Tyr Thr Pro Ser Ser Ser
   1490                1495                1500

ttc ggg gtg tct tcc tgc ttg ggt ggt cct ttg gag aaa ggc att tat   4560
Phe Gly Val Ser Ser Cys Leu Gly Gly Pro Leu Glu Lys Gly Ile Tyr
1505                1510                1515                1520

ttc tct gaa gaa gga ggt cat gtc gtc ttg gct cac tct gta ttg ttg   4608
Phe Ser Glu Glu Gly Gly His Val Val Leu Ala His Ser Val Leu Leu
               1525                1530                1535

ggg cca gaa ttt aag ctt gtt ttc agc atc cgc cca aga agt ctc act   4656
Gly Pro Glu Phe Lys Leu Val Phe Ser Ile Arg Pro Arg Ser Leu Thr
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          1540                1545                1550

ggg atc cta ata cac atc gga agt cag ccc ggg aag cac tta tgt gtt   4704
Gly Ile Leu Ile His Ile Gly Ser Gln Pro Gly Lys His Leu Cys Val
      1555                1560                1565

tac ctg gag gca gga aag gtc acg gcc tct atg gac agt ggg gca ggt   4752
Tyr Leu Glu Ala Gly Lys Val Thr Ala Ser Met Asp Ser Gly Ala Gly
   1570                1575                1580

ggg acc tca acg tcg gtc aca cca aag cag tct ctg tgt gat gga cag   4800
Gly Thr Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Gln
1585                1590                1595                1600

tgg cac tcg gtg gca gtc acc ata aaa caa cac atc ctg cac ctg gaa   4848
Trp His Ser Val Ala Val Thr Ile Lys Gln His Ile Leu His Leu Glu
               1605                1610                1615

ctg gac aca gac agt agc tac aca gct gga cag atc ccc ttc cca cct   4896
Leu Asp Thr Asp Ser Ser Tyr Thr Ala Gly Gln Ile Pro Phe Pro Pro
           1620                1625                1630

gcc agc act caa gag cca cta cac ctt gga ggt gct cca gcc aat ttg   4944
Ala Ser Thr Gln Glu Pro Leu His Leu Gly Gly Ala Pro Ala Asn Leu
       1635                1640                1645

acg aca ctg agg atc cct gtg tgg aaa tca ttc ttt ggc tgt ctg agg   4992
Thr Thr Leu Arg Ile Pro Val Trp Lys Ser Phe Phe Gly Cys Leu Arg
   1650                1655                1660

aat att cat gtc aat cac atc cct gtc cct gtc act gaa gcc ttg gaa   5040
Asn Ile His Val Asn His Ile Pro Val Pro Val Thr Glu Ala Leu Glu
1665                1670                1675                1680

gtc cag ggg cct gtc agt ctg aat ggt tgt cct gac cag taacccaagc    5089
Val Gln Gly Pro Val Ser Leu Asn Gly Cys Pro Asp Gln
               1685                1690

ctatttcaca gcaaggaaat tcaccttcaa aagcactgat tacccaatgc acctccctcc 5149

ccagctcgag atcattcttc aattaggaca caaaccagac aggtttaata gcgaatctaa 5209

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gtttttggta atattaattt ccactaaaaa attaaatgtc tttt                  5373


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Gln Gln Arg Val Pro Phe Leu Gln Pro Pro Gly Gln Ser Gln Leu Gln
  1               5                  10                  15

Ala Ser Tyr Val Glu Phe Arg Pro Ser Gln Gly Cys Ser Pro Gly Tyr
             20                  25                  30
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Tyr Arg Asp His Lys Gly Leu Tyr Thr Gly Arg Cys Val Pro Cys Asn
         35                  40                  45

Cys Asn Gly His Ser Asn Gln Cys Gln Asp Gly Ser Gly Ile Cys Val
     50                  55                  60

Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Gln Glu
 65                  70                  75                  80

Gly Tyr Tyr Gly Asn Ala Val His Gly Ser Cys Arg Ala Cys Pro Cys
                 85                  90                  95

Pro His Thr Asn Ser Phe Ala Thr Gly Cys Val Val Asn Gly Gly Asp
            100                 105                 110

Val Arg Cys Ser Cys Lys Ala Gly Tyr Thr Gly Thr Gln Cys Glu Arg
        115                 120                 125

Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys
    130                 135                 140

Gln Pro Cys Ser Cys Asn Ser Asn Gly Gln Leu Gly Ser Cys His Pro
145                 150                 155                 160

Leu Thr Gly Asp Cys Ile Asn Gln Glu Pro Lys Asp Ser Ser Pro Ala
                165                 170                 175

Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp
            180                 185                 190

Leu Ala Thr Met Gly Glu Gln Leu Arg Leu Val Lys Ser Gln Leu Gln
        195                 200                 205

Gly Leu Ser Ala Ser Ala Gly Leu Leu Glu Gln Met Arg His Met Glu
    210                 215                 220

Thr Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Asn Tyr Arg Ser Ala
225                 230                 235                 240

Ile Ser Asn His Gly Ser Lys Ile Glu Gly Leu Glu Arg Glu Leu Thr
                245                 250                 255

Asp Leu Asn Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn
            260                 265                 270

Ser Arg Lys Ala Gln Thr Leu Asn Asn Asn Val Asn Arg Ala Thr Gln
        275                 280                 285

Ser Ala Lys Glu Leu Asp Val Lys Ile Lys Asn Val Ile Arg Asn Val
    290                 295                 300

His Ile Leu Leu Lys Gln Ile Ser Gly Thr Asp Gly Glu Gly Asn Asn
305                 310                 315                 320

Val Pro Ser Gly Asp Phe Ser Arg Glu Trp Ala Glu Ala Gln Arg Met
                325                 330                 335

Met Arg Glu Leu Arg Asn Arg Asn Phe Gly Lys His Leu Arg Glu Ala
            340                 345                 350

Glu Ala Asp Lys Arg Glu Ser Gln Leu Leu Leu Asn Arg Ile Arg Thr
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        355                 360                 365

Trp Gln Lys Thr His Gln Gly Glu Asn Asn Gly Leu Ala Asn Ser Ile
    370                 375                 380

Arg Asp Ser Leu Asn Glu Tyr Glu Ala Lys Leu Ser Asp Leu Arg Ala
385                 390                 395                 400

Arg Leu Gln Glu Ala Ala Ala Gln Ala Lys Gln Ala Asn Gly Leu Asn
                405                 410                 415

Gln Glu Asn Glu Arg Ala Leu Gly Ala Ile Gln Arg Gln Val Lys Glu
            420                 425                 430

Ile Asn Ser Leu Gln Ser Asp Phe Thr Lys Tyr Leu Thr Thr Ala Asp
        435                 440                 445

Ser Ser Leu Leu Gln Thr Asn Ile Ala Leu Gln Leu Met Glu Lys Ser
    450                 455                 460

Gln Lys Glu Tyr Glu Lys Leu Ala Ala Ser Leu Asn Glu Ala Arg Gln
465                 470                 475                 480

Glu Leu Ser Asp Lys Val Arg Glu Leu Ser Arg Ser Ala Gly Lys Thr
                485                 490                 495

Ser Leu Val Glu Glu Ala Glu Lys His Ala Arg Ser Leu Gln Glu Leu
            500                 505                 510

Ala Lys Gln Leu Glu Glu Ile Lys Arg Asn Ala Ser Gly Asp Glu Leu
        515                 520                 525

Val Arg Cys Ala Val Asp Ala Ala Thr Ala Tyr Glu Asn Ile Leu Asn
    530                 535                 540

Ala Ile Lys Ala Ala Glu Asp Ala Ala Asn Arg Ala Ala Ser Ala Ser
545                 550                 555                 560

Glu Ser Ala Leu Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Lys Ala
                565                 570                 575

Lys Thr Leu Ser Ser Asn Ser Asp Lys Leu Leu Asn Glu Ala Lys Met
            580                 585                 590

Thr Gln Lys Lys Leu Lys Gln Glu Val Ser Pro Ala Leu Asn Asn Leu
        595                 600                 605

Gln Gln Thr Leu Asn Ile Val Thr Val Gln Lys Glu Val Ile Asp Thr
    610                 615                 620

Asn Leu Thr Thr Leu Arg Asp Gly Leu His Gly Ile Gln Arg Gly Asp
625                 630                 635                 640

Ile Asp Ala Met Ile Ser Ser Ala Lys Ser Met Val Arg Lys Ala Asn
                645                 650                 655

Asp Ile Thr Asp Glu Val Leu Asp Gly Leu Asn Pro Ile Gln Thr Asp
            660                 665                 670

Val Glu Arg Ile Lys Asp Thr Tyr Gly Arg Thr Gln Asn Glu Asp Phe
        675                 680                 685
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Lys Lys Ala Leu Thr Asp Ala Asp Asn Ser Val Asn Lys Leu Thr Asn
    690                 695                 700

Lys Leu Pro Asp Leu Trp Arg Lys Ile Glu Ser Ile Asn Gln Gln Leu
705                 710                 715                 720

Leu Pro Leu Gly Asn Ile Ser Asp Asn Met Asp Arg Ile Arg Glu Leu
                725                 730                 735

Ile Gln Gln Ala Arg Asp Ala Ala Ser Lys Val Ala Val Pro Met Arg
            740                 745                 750

Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu
        755                 760                 765

Asp Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asn
    770                 775                 780

Ser Arg Glu Asn Gly Gly Thr Glu Asn Met Phe Val Met Tyr Leu Gly
785                 790                 795                 800

Asn Lys Asp Ala Ser Arg Asp Tyr Ile Gly Met Ala Val Val Asp Gly
                805                 810                 815

Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Leu Gln
            820                 825                 830

Val Asp Gln Ile Leu Thr Lys Ser Glu Thr Lys Glu Ala Val Met Asp
        835                 840                 845

Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Arg Leu Asn Tyr Thr
    850                 855                 860

Lys Gly Ala Thr Ser Ser Lys Pro Glu Thr Pro Gly Val Tyr Asp Met
865                 870                 875                 880

Asp Gly Arg Asn Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asn Val
                885                 890                 895

Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Lys Leu Pro Ser Arg
            900                 905                 910

Leu Ser Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn
        915                 920                 925

Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Lys Thr Phe Asn Leu Asn
    930                 935                 940

Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys
945                 950                 955                 960

Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Val Pro Thr Gln Pro His
                965                 970                 975

Ala Pro Ile Pro Thr Phe Gly Gln Thr Ile Gln Thr Thr Val Asp Arg
            980                 985                 990

Gly Leu Leu Phe Phe Ala Glu Asn Gly Asp Arg Phe Il  Ser Leu Asn
        995                1000                1005
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Ile Glu Asp Gly Lys Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Leu
1010 1015 1020

Pro Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn Gly Arg Asp His
1025 1030 1035 1040

Ser Ile Gln Ile Lys Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn
1045 1050 1055

Val Asp Val Gln Asn Thr Ile Ile Asp Gly Glu Val Phe Asp Phe Ser
1060 1065 1070

Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn
1075 1080 1085

Ile Ser Thr Pro Ala Phe Arg Gly Cys Met Lys Asn Leu Lys Lys Thr
1090 1095 1100

Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys
1105 1110 1115 1120

Ser Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe Ser Arg Gly Gly
1125 1130 1135

Gln Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr Asp His Leu Gln
1140 1145 1150

Ala Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Ile Leu Leu Asp
1155 1160 1165

His Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu Glu Asp Gly Tyr
1170 1175 1180

Ile Glu Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile Phe Lys Ser Pro
1185 1190 1195 1200

Gln Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser Val Ile Ser Asp
1205 1210 1215

Asn Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu Leu Arg Asn Ser
1220 1225 1230

Lys Arg Leu Lys His Ile Ser Ser Ser Arg Gln Ser Leu Arg Leu Gly
1235 1240 1245

Gly Ser Asn Phe Glu Gly Cys Ile Ser Asn Val Phe Val Gln Arg Leu
1250 1255 1260

Ser Leu Ser Pro Glu Val Leu Asp Leu Thr Ser Asn Ser Leu Lys Arg
1265 1270 1275 1280

Asp Val Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met
1285 1290 1295

Leu Leu Lys Gly Ser Thr Arg Phe Asn Lys Thr Lys Thr Phe Arg Ile
1300 1305 1310

Asn Gln Leu Leu Gln Asp Thr Pro Val Ala Ser Pro Arg Ser Val Lys
1315 1320 1325

Val Trp Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr Gln Ala Asn His

1330 1335 1340

Gly Ala Leu Gln Phe Gly Asp Ile Pro Thr Ser His Leu Leu Phe Lys
1345 1350 1355 1360

Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ala Val Asp Met
1365 1370 1375

Gln Thr Thr Ser Ser Arg Gly Leu Val Phe His Thr Gly Thr Lys Asn
1380 1385 1390

Ser Phe Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu Val Phe Ala Leu
1395 1400 1405

Gly Thr Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys Glu Lys Cys Asn
1410 1415 1420

Asp Gly Lys Trp His Thr Val Val Phe Gly His Asp Gly Glu Lys Gly
1425 1430 1435 1440

Arg Leu Val Val Asp Gly Leu Arg Ala Arg Glu Gly Ser Leu Pro Gly
1445 1450 1455

Asn Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu Gly Ser Pro Pro
1460 1465 1470

Ser Gly Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe Val Gly Cys Leu
1475 1480 1485

Lys Asn Phe Gln Leu Asp Ser Lys Pro Leu Tyr Thr Pro Ser Ser Ser
1490 1495 1500

Phe Gly Val Ser Ser Cys Leu Gly Gly Pro Leu Glu Lys Gly Ile Tyr
1505 1510 1515 1520

Phe Ser Glu Glu Gly Gly His Val Val Leu Ala His Ser Val Leu Leu
1525 1530 1535

Gly Pro Glu Phe Lys Leu Val Phe Ser Ile Arg Pro Arg Ser Leu Thr
1540 1545 1550

Gly Ile Leu Ile His Ile Gly Ser Gln Pro Gly Lys His Leu Cys Val
1555 1560 1565

Tyr Leu Glu Ala Gly Lys Val Thr Ala Ser Met Asp Ser Gly Ala Gly
1570 1575 1580

Gly Thr Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Gln
1585 1590 1595 1600

Trp His Ser Val Ala Val Thr Ile Lys Gln His Ile Leu His Leu Glu
1605 1610 1615

Leu Asp Thr Asp Ser Ser Tyr Thr Ala Gly Gln Ile Pro Phe Pro Pro
1620 1625 1630

Ala Ser Thr Gln Glu Pro Leu His Leu Gly Gly Ala Pro Ala Asn Leu
1635 1640 1645

Thr Thr Leu Arg Ile Pro Val Trp Lys Ser Phe Phe Gly Cys Leu Arg
1650 1655 1660

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Asn Ile His Val Asn His Ile Pro Val Pro Val Thr Glu Ala Leu Glu
1665                1670                1675                1680

Val Gln Gly Pro Val Ser Leu Asn Gly Cys Pro Asp Gln
                1685                1690
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atg ccg cct aca gtg agg tgg tca gcc tgg tgc aca gga tgg ctg tgg    106
Met Pro Pro Thr Val Arg Trp Ser Ala Trp Cys Thr Gly Trp Leu Trp
  1               5                  10                  15

atc ttt ggg gca gct ctg ggc cag tgc ctg ggg tat ggc tca gag cag    154
Ile Phe Gly Ala Ala Leu Gly Gln Cys Leu Gly Tyr Gly Ser Glu Gln
            20                  25                  30

caa agg gta gca ttt ctt cag cat cca ggg caa aac cat ctg caa gca    202
Gln Arg Val Ala Phe Leu Gln His Pro Gly Gln Asn His Leu Gln Ala
        35                  40                  45

agt tat atg gag ctt aga ccc agc cag ggc tgt cgc cca gga tac tat    250
Ser Tyr Met Glu Leu Arg Pro Ser Gln Gly Cys Arg Pro Gly Tyr Tyr
    50                  55                  60

cga gac atc aaa agc ttc cct gcg gga agg tct gtt ccc tgc aat tgc    298
Arg Asp Ile Lys Ser Phe Pro Ala Gly Arg Ser Val Pro Cys Asn Cys
65                  70                  75                  80

aac gga cat tca aat aga tgc caa gac ggc tcg gga gtg tgc att aac    346
Asn Gly His Ser Asn Arg Cys Gln Asp Gly Ser Gly Val Cys Ile Asn
                85                  90                  95

tgt cag cac aac aca gct ggg gag cac tgt gag cgt tgc aag agg ggt    394
Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Lys Arg Gly
            100                 105                 110

tac tat gga agc gcc atc cat gga tcc tgc agg gtt tgc ccc tgt cct    442
Tyr Tyr Gly Ser Ala Ile His Gly Ser Cys Arg Val Cys Pro Cys Pro
        115                 120                 125

cac acc aac agc ttt gcc act ggc tgt gct gtg gat gga gga gct gtg    490
His Thr Asn Ser Phe Ala Thr Gly Cys Ala Val Asp Gly Gly Ala Val
    130                 135                 140

agg tgt gcc tgc aaa ccc gga tac aca gga gca cag tgt gag agg tgt    538
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Arg Cys Ala Cys Lys Pro Gly Tyr Thr Gly Ala Gln Cys Glu Arg Cys
145                 150                 155                 160

gca cca gga tat ttt ggg aac ccc cag aaa ttt gga ggt agc tgc caa   586
Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys Gln
                165                 170                 175

cca tgc aat tgc aac agt aat ggc cag ttt ggc act tgt gat ccc cta   634
Pro Cys Asn Cys Asn Ser Asn Gly Gln Phe Gly Thr Cys Asp Pro Leu
            180                 185                 190

act gga gac tgt gta agc caa gaa ccc aaa gat ggc agc cct gca gaa   682
Thr Gly Asp Cys Val Ser Gln Glu Pro Lys Asp Gly Ser Pro Ala Glu
        195                 200                 205

gaa tgt gat gac tgt gac agc tgt gtg atg act ctc cta aat gac ttg   730
Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp Leu
    210                 215                 220

gtc ccc atg ggt gag gaa ctc gcc ctg gtg aaa tca aaa ctt cag ggg   778
Val Pro Met Gly Glu Glu Leu Ala Leu Val Lys Ser Lys Leu Gln Gly
225                 230                 235                 240

ctg agt gtg aac act ggt tct ctg gaa cag atc cgg cat gtg gag atg   826
Leu Ser Val Asn Thr Gly Ser Leu Glu Gln Ile Arg His Val Glu Met
                245                 250                 255

cag gcc aag gac ctg agg aac cag ctg ctt ggc ttc cgt tcc gcc atc   874
Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Gly Phe Arg Ser Ala Ile
            260                 265                 270

tcc agt cac ggg tcc caa atg gac ggc ctg gaa aaa gaa ctc agt cat   922
Ser Ser His Gly Ser Gln Met Asp Gly Leu Glu Lys Glu Leu Ser His
        275                 280                 285

ttg tac cag gaa ttc gaa act ttg caa gaa aag gcg cag gtc aat tcc   970
Leu Tyr Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn Ser
    290                 295                 300

aga aaa gca caa aca tta tat aac aac atc gat acg aca atc caa aac   1018
Arg Lys Ala Gln Thr Leu Tyr Asn Asn Ile Asp Thr Thr Ile Gln Asn
305                 310                 315                 320

gcc aaa gag ttg gac atg aag att aaa aac ata ctt acg aat gtg cac   1066
Ala Lys Glu Leu Asp Met Lys Ile Lys Asn Ile Leu Thr Asn Val His
                325                 330                 335

att ctc ctg aag cag atc gct cgg cca ggt gga gaa gga atg gac ttg   1114
Ile Leu Leu Lys Gln Ile Ala Arg Pro Gly Gly Glu Gly Met Asp Leu
            340                 345                 350

ccg gtg ggc gac tgg tcc agg gag tcg gcg gaa gct cag cgc atg ttg   1162
Pro Val Gly Asp Trp Ser Arg Glu Ser Ala Glu Ala Gln Arg Met Leu
        355                 360                 365

cgg gag ctg cga ggc cga gac ttt aaa aag cac ctc caa gaa gca gag   1210
Arg Glu Leu Arg Gly Arg Asp Phe Lys Lys His Leu Gln Glu Ala Glu
    370                 375                 380

gcc cag aaa atg gaa gcc cag ctc tta ctg aac cga atc agg acc tgg   1258
Ala Gln Lys Met Glu Ala Gln Leu Leu Leu Asn Arg Ile Arg Thr Trp
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385                 390                 395                 400

ctg gaa tcc cac cag gtg gag aac aat gga ctg cta aag aat att cgg   1306
Leu Glu Ser His Gln Val Glu Asn Asn Gly Leu Leu Lys Asn Ile Arg
                405                 410                 415

gat tca tta aat gat tat gaa gcc aaa ctt cag gac ctg cgt tcc gtg   1354
Asp Ser Leu Asn Asp Tyr Glu Ala Lys Leu Gln Asp Leu Arg Ser Val
            420                 425                 430

ctt cag gag gcg gca gcc cag gga aag cag gct aca ggc ctc aac cac   1402
Leu Gln Glu Ala Ala Ala Gln Gly Lys Gln Ala Thr Gly Leu Asn His
        435                 440                 445

gaa aat gag ggg gtc cta gga gcc atc cag aga caa atg aag gaa atg   1450
Glu Asn Glu Gly Val Leu Gly Ala Ile Gln Arg Gln Met Lys Glu Met
    450                 455                 460

gat tcc ctg aag aag tac ctc acc gag cac ctg gcc aca gca gac gct   1498
Asp Ser Leu Lys Lys Tyr Leu Thr Glu His Leu Ala Thr Ala Asp Ala
465                 470                 475                 480

tcc ctg ctg caa acc aac agt cta ctg cag cgg atg gac acg agc cag   1546
Ser Leu Leu Gln Thr Asn Ser Leu Leu Gln Arg Met Asp Thr Ser Gln
                485                 490                 495

aag gag tat gaa agc tta gct gct gct tta aac gga gca aga cag gaa   1594
Lys Glu Tyr Glu Ser Leu Ala Ala Ala Leu Asn Gly Ala Arg Gln Glu
            500                 505                 510

ctg aat gac caa gtg cgg gaa ctc tcc aga tcc gga ggc aaa gca ccc   1642
Leu Asn Asp Gln Val Arg Glu Leu Ser Arg Ser Gly Gly Lys Ala Pro
        515                 520                 525

ctg gtg gct gag gcc gag aag cac gct cag tct tta cag gag ctg gca   1690
Leu Val Ala Glu Ala Glu Lys His Ala Gln Ser Leu Gln Glu Leu Ala
    530                 535                 540

aag cag ctg gaa gag ata aag aga aac acc agt ggg gat gag tcg gtg   1738
Lys Gln Leu Glu Glu Ile Lys Arg Asn Thr Ser Gly Asp Glu Ser Val
545                 550                 555                 560

cgc tgt gtc gtg gac gct gcc act gcc tat gag agc atc ctc aac gcc   1786
Arg Cys Val Val Asp Ala Ala Thr Ala Tyr Glu Ser Ile Leu Asn Ala
                565                 570                 575

atc cga gca gca gag gat gca gcc ggc aag gcc gac agt gcc tca gag   1834
Ile Arg Ala Ala Glu Asp Ala Ala Gly Lys Ala Asp Ser Ala Ser Glu
            580                 585                 590

tcc gcc ttc cag aca gtg ata aag gaa gat ctt ccg aga aga gcc aaa   1882
Ser Ala Phe Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Arg Ala Lys
        595                 600                 605

acc ctg agt tct gac agc gag gaa ctg tta aac gag gcc aag atg aca   1930
Thr Leu Ser Ser Asp Ser Glu Glu Leu Leu Asn Glu Ala Lys Met Thr
    610                 615                 620

cgg aaa agg cta cag caa gaa atc aat cca gct ctc aac agc cta cag   1978
Arg Lys Arg Leu Gln Gln Glu Ile Asn Pro Ala Leu Asn Ser Leu Gln
625                 630                 635                 640
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caa acc ctg aag act gta tca gtt cag aag gac ctg cta gat gcc aat   2026
Gln Thr Leu Lys Thr Val Ser Val Gln Lys Asp Leu Leu Asp Ala Asn
                645                 650                 655

gtc act gct gtc cgt aat gac ctt cgt ggg atc cag aga ggt gat att   2074
Val Thr Ala Val Arg Asn Asp Leu Arg Gly Ile Gln Arg Gly Asp Ile
            660                 665                 670

gac agt gtg gtg agt gga gcg aag agc atg gtc agg aaa gcc aat ggg   2122
Asp Ser Val Val Ser Gly Ala Lys Ser Met Val Arg Lys Ala Asn Gly
        675                 680                 685

ata acg agc gag gtc ctg gac ggg ctc agc ccc atc cag acg gat ttg   2170
Ile Thr Ser Glu Val Leu Asp Gly Leu Ser Pro Ile Gln Thr Asp Leu
    690                 695                 700

gga agg att aag gac agc tac ggg agc aca cgg cat gag gac ttc aac   2218
Gly Arg Ile Lys Asp Ser Tyr Gly Ser Thr Arg His Glu Asp Phe Asn
705                 710                 715                 720

aaa gct ctg att gac gcc aat aac tca gta aag aaa tta acc aag aag   2266
Lys Ala Leu Ile Asp Ala Asn Asn Ser Val Lys Lys Leu Thr Lys Lys
                725                 730                 735

ttg cct gat ctt ttt gtc aag att gaa agc atc aat caa cag ttg ctg   2314
Leu Pro Asp Leu Phe Val Lys Ile Glu Ser Ile Asn Gln Gln Leu Leu
            740                 745                 750

ccc ctg gga aac atc tct gac aat gta gac cga atc cga gag ctc att   2362
Pro Leu Gly Asn Ile Ser Asp Asn Val Asp Arg Ile Arg Glu Leu Ile
        755                 760                 765

acg cag gcc aga gat gct gcg aac aag gtt gca att ccc atg agg ttc   2410
Thr Gln Ala Arg Asp Ala Ala Asn Lys Val Ala Ile Pro Met Arg Phe
    770                 775                 780

aat ggt aaa tct ggt gtt gaa gtc cgt ctg cca aat gac cta gaa gac   2458
Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu Asp
785                 790                 795                 800

ttg aag gga tac acg tct ctg tct ttg ttc ctc caa aga cca gac tta   2506
Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asp Leu
                805                 810                 815

aga gag aat gga ggc act gag gac atg ttt gta atg tac ctt gga aac   2554
Arg Glu Asn Gly Gly Thr Glu Asp Met Phe Val Met Tyr Leu Gly Asn
            820                 825                 830

aag gat gcc tcc aag gac tac atc ggc atg gcg gtt gta gat ggc cag   2602
Lys Asp Ala Ser Lys Asp Tyr Ile Gly Met Ala Val Val Asp Gly Gln
        835                 840                 845

ctg acg tgt gtc tac aac ctg ggg gac cga gaa gct gaa gtt cag atc   2650
Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Val Gln Ile
    850                 855                 860

gat cag gtc ctg acg gag agt gag tct cag gag gca gtt atg gac cgg   2698
Asp Gln Val Leu Thr Glu Ser Glu Ser Gln Glu Ala Val Met Asp Arg
865                 870                 875                 880
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gtg aag ttc cag aga ata tat caa ttt gcc aag ctt aat tac acc aaa   2746
Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Lys Leu Asn Tyr Thr Lys
                885                 890                 895

gaa gcc acg tcc aat aaa ccc aaa gct ccc gcg gtc tac gac ctg gag   2794
Glu Ala Thr Ser Asn Lys Pro Lys Ala Pro Ala Val Tyr Asp Leu Glu
            900                 905                 910

ggt ggc agt agc aac acg ctc ctt aat ttg gat ccc gag gac gct gtg   2842
Gly Gly Ser Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asp Ala Val
        915                 920                 925

ttt tat gtc gga ggt tac cca ccg gat ttt gaa ctt cct agc aga ctg   2890
Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Glu Leu Pro Ser Arg Leu
    930                 935                 940

cgg ttc cct cca tac aaa ggc tgt atc gaa cta gat gac ctc aat gaa   2938
Arg Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn Glu
945                 950                 955                 960

aac gtt cta agc ttg tac aat ttc aag aca act ttc aat ctc aac acc   2986
Asn Val Leu Ser Leu Tyr Asn Phe Lys Thr Thr Phe Asn Leu Asn Thr
                965                 970                 975

acg gag gtg gag cct tgt agg agg aga aag gaa gag tca gac aaa aat   3034
Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys Asn
            980                 985                 990

tac ttt gaa ggt aca ggc tat gct cgc atc cct act caa cca aat gct   3082
Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Ile Pro Thr Gln Pro Asn Ala
        995                1000                1005

ccc ttc cca aac ttc ata cag acc atc cag act act gtg gac aga ggt   3130
Pro Phe Pro Asn Phe Ile Gln Thr Ile Gln Thr Thr Val Asp Arg Gly
   1010                1015                1020

tta ctg ttc ttc gca gaa aac cag gat aac ttc ata tct ctg aac ata   3178
Leu Leu Phe Phe Ala Glu Asn Gln Asp Asn Phe Ile Ser Leu Asn Ile
1025                1030                1035                1040

gaa gat ggc aat ctc atg gtg aga tac aaa cta aat tca gag cca ccc   3226
Glu Asp Gly Asn Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Pro Pro
                1045                1050                1055

aaa gag aag gga att cga gac acc atc aac gat ggg aaa gat cat tcg   3274
Lys Glu Lys Gly Ile Arg Asp Thr Ile Asn Asp Gly Lys Asp His Ser
            1060                1065                1070

atc tta atc aca att gga aaa cta caa aaa cgc atg tgg ata aat gtg   3322
Ile Leu Ile Thr Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn Val
        1075                1080                1085

aac gaa cgc agt gta cga atc gaa ggg gaa ata ttt gat ttc agc aca   3370
Asn Glu Arg Ser Val Arg Ile Glu Gly Glu Ile Phe Asp Phe Ser Thr
   1090                1095                1100

tat tat ttg ggc gga att cca att gca atc aga gaa agg ttt aac atc   3418
Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn Ile
1105                1110                1115                1120

tca acg cct gct ttc caa ggc tgc atg aag aat ctg aag aaa acc agt   3466
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Ser Thr Pro Ala Phe Gln Gly Cys Met Lys Asn Leu Lys Lys Thr Ser
                1125                1130                1135

ggg gtt gtc agg ttg aat gat act gtg ggt gta acc aag aag tgc tca   3514
Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys Ser
            1140                1145                1150

gaa gac tgg aag ctt gtg cga acc gcc tcg ttc tcc aga gga ggg cag   3562
Glu Asp Trp Lys Leu Val Arg Thr Ala Ser Phe Ser Arg Gly Gly Gln
        1155                1160                1165

atg agc ttt aca aac ttg gac gtg ccc tcg act gac cgc ttc cag ctc   3610
Met Ser Phe Thr Asn Leu Asp Val Pro Ser Thr Asp Arg Phe Gln Leu
    1170                1175                1180

tcc ttt ggg ttt cag acc ttt caa ccc agt ggc aca ctg ctc aat cat   3658
Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Thr Leu Leu Asn His
1185                1190                1195                1200

cag acg cgg aca agc agc ctg ctg gtc acc ctg gaa gat ggg cac att   3706
Gln Thr Arg Thr Ser Ser Leu Leu Val Thr Leu Glu Asp Gly His Ile
                1205                1210                1215

gag ttg agc act agg gac agc aac atc cca att ttc aag tct cca ggg   3754
Glu Leu Ser Thr Arg Asp Ser Asn Ile Pro Ile Phe Lys Ser Pro Gly
            1220                1225                1230

acc tac atg gac ggt tta ctg cat cat gta tct gta ata agt gac acc   3802
Thr Tyr Met Asp Gly Leu Leu His His Val Ser Val Ile Ser Asp Thr
        1235                1240                1245

tca ggt ctc cgc ctt ctc atc gat gac cag gtc ctg aga agg aac cag   3850
Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Val Leu Arg Arg Asn Gln
    1250                1255                1260

agg ctt cct agc ttc tct aac gcc cag cag tcg ctc cgc ctt gga gga   3898
Arg Leu Pro Ser Phe Ser Asn Ala Gln Gln Ser Leu Arg Leu Gly Gly
1265                1270                1275                1280

ggt cat ttc gag ggt tgt atc agc aat gtt tta gtc caa agg ttt tca   3946
Gly His Phe Glu Gly Cys Ile Ser Asn Val Leu Val Gln Arg Phe Ser
                1285                1290                1295

cag agt cca gaa gtc ctg gat ctg gcc agt aaa tct acc aag aag gat   3994
Gln Ser Pro Glu Val Leu Asp Leu Ala Ser Lys Ser Thr Lys Lys Asp
            1300                1305                1310

gca tcc cta gga ggc tgc agt tta aac aag cca cct ttt ctt atg ttg   4042
Ala Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met Leu
        1315                1320                1325

ttt aaa agt ccc aag aga ttt aac aag ggc cgg att ttc aat gtt aat   4090
Phe Lys Ser Pro Lys Arg Phe Asn Lys Gly Arg Ile Phe Asn Val Asn
    1330                1335                1340

cag ctg atg caa gat gca cct cag gcc aca agg agc aca gag gct tgg   4138
Gln Leu Met Gln Asp Ala Pro Gln Ala Thr Arg Ser Thr Glu Ala Trp
1345                1350                1355                1360

caa gat ggg agg tcc tgc cta cca cct ctg aac acc aag gcc tct cac   4186
Gln Asp Gly Arg Ser Cys Leu Pro Pro Leu Asn Thr Lys Ala Ser His
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                1365                1370                1375

aga gcc ctg cag ttt gga gac agc ccc acc agc cac ttg cta ctc aag   4234
Arg Ala Leu Gln Phe Gly Asp Ser Pro Thr Ser His Leu Leu Leu Lys
            1380                1385                1390

ctt ccc cag gaa ctg ctg aaa cct agg tca cag ttt tct tta gac ata   4282
Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ser Leu Asp Ile
        1395                1400                1405

cag aca act tcc ccc aaa gga ctg gtg ttt tac gca ggc acc aag gac   4330
Gln Thr Thr Ser Pro Lys Gly Leu Val Phe Tyr Ala Gly Thr Lys Asp
    1410                1415                1420

tcc ttc ctg gct ctt tat gtc gca gat ggc cgt gtt gtc ttt gct ttg   4378
Ser Phe Leu Ala Leu Tyr Val Ala Asp Gly Arg Val Val Phe Ala Leu
1425                1430                1435                1440

ggg gca gga ggg aag aaa ctg aga ctc agg agc aag gag aga tac cat   4426
Gly Ala Gly Gly Lys Lys Leu Arg Leu Arg Ser Lys Glu Arg Tyr His
                1445                1450                1455

gac ggg aag tgg cac acg gtg gtg ttc gga cta aat gga gga aag gca   4474
Asp Gly Lys Trp His Thr Val Val Phe Gly Leu Asn Gly Gly Lys Ala
            1460                1465                1470

cgc ctg gtt gtg gat ggg cta agg gcc cag gaa ggc agt ttg cct gga   4522
Arg Leu Val Val Asp Gly Leu Arg Ala Gln Glu Gly Ser Leu Pro Gly
        1475                1480                1485

aat tct acc atc agc ccc aga gaa cag gtt tac cta ggg ttg ccg cta   4570
Asn Ser Thr Ile Ser Pro Arg Glu Gln Val Tyr Leu Gly Leu Pro Leu
    1490                1495                1500

tca aga aag cca aag agc cta ccc cag cac agt ttt gtg ggg tgc ctg   4618
Ser Arg Lys Pro Lys Ser Leu Pro Gln His Ser Phe Val Gly Cys Leu
1505                1510                1515                1520

aga gat ttc cag ttg aac tcg aaa ccc ctg gat tct cct tct gcg agg   4666
Arg Asp Phe Gln Leu Asn Ser Lys Pro Leu Asp Ser Pro Ser Ala Arg
                1525                1530                1535

ttt ggg gta tct ccc tgc ttg ggt ggc tct tta gag aaa ggc att tat   4714
Phe Gly Val Ser Pro Cys Leu Gly Gly Ser Leu Glu Lys Gly Ile Tyr
            1540                1545                1550

ttc tcc caa gga gga ggc cat gtg atc cta gcc aat tct gtg tcc ttg   4762
Phe Ser Gln Gly Gly Gly His Val Ile Leu Ala Asn Ser Val Ser Leu
        1555                1560                1565

ggg cca gag ctt aag ctc act ttc agc att cgc cca cgg agt ctc act   4810
Gly Pro Glu Leu Lys Leu Thr Phe Ser Ile Arg Pro Arg Ser Leu Thr
    1570                1575                1580

ggg gtc tta ata cac gtc gga agt caa tct gga cag cgc tta agt gtg   4858
Gly Val Leu Ile His Val Gly Ser Gln Ser Gly Gln Arg Leu Ser Val
1585                1590                1595                1600

tac atg gag gca gga aag gtc aca acc tct gtg agc agt gat gca gga   4906
Tyr Met Glu Ala Gly Lys Val Thr Thr Ser Val Ser Ser Asp Ala Gly
                1605                1610                1615
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gga agt gtg aca tca att aca ccg aag cag tct ctg tgt gat gga cag   4954
Gly Ser Val Thr Ser Ile Thr Pro Lys Gln Ser Leu Cys Asp Gly Gln
          1620                1625                1630

tgg cac tcg gtg gca gtc tcc att aaa cag cgc atc ctg cat cta gaa   5002
Trp His Ser Val Ala Val Ser Ile Lys Gln Arg Ile Leu His Leu Glu
       1635                1640                1645

ctg gat aca gac agt agc tac aca gtc gca cca ctt tcc ttc tca cca   5050
Leu Asp Thr Asp Ser Ser Tyr Thr Val Ala Pro Leu Ser Phe Ser Pro
   1650                1655                1660

aac agc acc cga ggg tca ctg cac gtc gga ggt gtc cca gac aaa ttg   5098
Asn Ser Thr Arg Gly Ser Leu His Val Gly Gly Val Pro Asp Lys Leu
1665                1670                1675                1680

aaa atg ctt aca ctc cct gtg tgg aac tca ttt ttt ggc tgt ctg aag   5146
Lys Met Leu Thr Leu Pro Val Trp Asn Ser Phe Phe Gly Cys Leu Lys
              1685                1690                1695

aat att caa gtc aac cat gtc cct gtc ccc atc aca gaa gcc aca gaa   5194
Asn Ile Gln Val Asn His Val Pro Val Pro Ile Thr Glu Ala Thr Glu
          1700                1705                1710

gtc caa ggt tct gtc agc ctg aat ggc tgc cct gac cac taaccctaca   5243
Val Gln Gly Ser Val Ser Leu Asn Gly Cys Pro Asp His
       1715                1720                1725

cagcaagatt caccttgga g                                          5264
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Met Pro Pro Thr Val Arg Trp Ser Ala Trp Cys Thr Gly Trp Leu Trp
  1               5                  10                  15

Ile Phe Gly Ala Ala Leu Gly Gln Cys Leu Gly Tyr Gly Ser Glu Gln
             20                  25                  30

Gln Arg Val Ala Phe Leu Gln His Pro Gly Gln Asn His Leu Gln Ala
         35                  40                  45

Ser Tyr Met Glu Leu Arg Pro Ser Gln Gly Cys Arg Pro Gly Tyr Tyr
     50                  55                  60

Arg Asp Ile Lys Ser Phe Pro Ala Gly Arg Ser Val Pro Cys Asn Cys
 65                  70                  75                  80

Asn Gly His Ser Asn Arg Cys Gln Asp Gly Ser Gly Val Cys Ile Asn
                 85                  90                  95

Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Lys Arg Gly
            100                 105                 110

Tyr Tyr Gly Ser Ala Ile His Gly Ser Cys Arg Val Cys Pro Cys Pro
        115                 120                 125
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His Thr Asn Ser Phe Ala Thr Gly Cys Ala Val Asp Gly Gly Ala Val
    130                 135                 140

Arg Cys Ala Cys Lys Pro Gly Tyr Thr Gly Ala Gln Cys Glu Arg Cys
145                 150                 155                 160

Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys Gln
                165                 170                 175

Pro Cys Asn Cys Asn Ser Asn Gly Gln Phe Gly Thr Cys Asp Pro Leu
            180                 185                 190

Thr Gly Asp Cys Val Ser Gln Glu Pro Lys Asp Gly Ser Pro Ala Glu
        195                 200                 205

Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp Leu
    210                 215                 220

Val Pro Met Gly Glu Glu Leu Ala Leu Val Lys Ser Lys Leu Gln Gly
225                 230                 235                 240

Leu Ser Val Asn Thr Gly Ser Leu Glu Gln Ile Arg His Val Glu Met
                245                 250                 255

Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Gly Phe Arg Ser Ala Ile
            260                 265                 270

Ser Ser His Gly Ser Gln Met Asp Gly Leu Glu Lys Glu Leu Ser His
        275                 280                 285

Leu Tyr Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn Ser
    290                 295                 300

Arg Lys Ala Gln Thr Leu Tyr Asn Asn Ile Asp Thr Thr Ile Gln Asn
305                 310                 315                 320

Ala Lys Glu Leu Asp Met Lys Ile Lys Asn Ile Leu Thr Asn Val His
                325                 330                 335

Ile Leu Leu Lys Gln Ile Ala Arg Pro Gly Gly Glu Gly Met Asp Leu
            340                 345                 350

Pro Val Gly Asp Trp Ser Arg Glu Ser Ala Glu Ala Gln Arg Met Leu
        355                 360                 365

Arg Glu Leu Arg Gly Arg Asp Phe Lys Lys His Leu Gln Glu Ala Glu
    370                 375                 380

Ala Gln Lys Met Glu Ala Gln Leu Leu Leu Asn Arg Ile Arg Thr Trp
385                 390                 395                 400

Leu Glu Ser His Gln Val Glu Asn Asn Gly Leu Leu Lys Asn Ile Arg
                405                 410                 415

Asp Ser Leu Asn Asp Tyr Glu Ala Lys Leu Gln Asp Leu Arg Ser Val
            420                 425                 430

Leu Gln Glu Ala Ala Ala Gln Gly Lys Gln Ala Thr Gly Leu Asn His
        435                 440                 445
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Glu Asn Glu Gly Val Leu Gly Ala Ile Gln Arg Gln Met Lys Glu Met
    450                 455                 460

Asp Ser Leu Lys Lys Tyr Leu Thr Glu His Leu Ala Thr Ala Asp Ala
465                 470                 475                 480

Ser Leu Leu Gln Thr Asn Ser Leu Leu Gln Arg Met Asp Thr Ser Gln
                485                 490                 495

Lys Glu Tyr Glu Ser Leu Ala Ala Ala Leu Asn Gly Ala Arg Gln Glu
            500                 505                 510

Leu Asn Asp Gln Val Arg Glu Leu Ser Arg Ser Gly Gly Lys Ala Pro
        515                 520                 525

Leu Val Ala Glu Ala Glu Lys His Ala Gln Ser Leu Gln Glu Leu Ala
    530                 535                 540

Lys Gln Leu Glu Glu Ile Lys Arg Asn Thr Ser Gly Asp Glu Ser Val
545                 550                 555                 560

Arg Cys Val Val Asp Ala Ala Thr Ala Tyr Glu Ser Ile Leu Asn Ala
                565                 570                 575

Ile Arg Ala Ala Glu Asp Ala Ala Gly Lys Ala Asp Ser Ala Ser Glu
            580                 585                 590

Ser Ala Phe Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Arg Ala Lys
        595                 600                 605

Thr Leu Ser Ser Asp Ser Glu Glu Leu Leu Asn Glu Ala Lys Met Thr
    610                 615                 620

Arg Lys Arg Leu Gln Gln Glu Ile Asn Pro Ala Leu Asn Ser Leu Gln
625                 630                 635                 640

Gln Thr Leu Lys Thr Val Ser Val Gln Lys Asp Leu Leu Asp Ala Asn
                645                 650                 655

Val Thr Ala Val Arg Asn Asp Leu Arg Gly Ile Gln Arg Gly Asp Ile
            660                 665                 670

Asp Ser Val Val Ser Gly Ala Lys Ser Met Val Arg Lys Ala Asn Gly
        675                 680                 685

Ile Thr Ser Glu Val Leu Asp Gly Leu Ser Pro Ile Gln Thr Asp Leu
    690                 695                 700

Gly Arg Ile Lys Asp Ser Tyr Gly Ser Thr Arg His Glu Asp Phe Asn
705                 710                 715                 720

Lys Ala Leu Ile Asp Ala Asn Asn Ser Val Lys Lys Leu Thr Lys Lys
                725                 730                 735

Leu Pro Asp Leu Phe Val Lys Ile Glu Ser Ile Asn Gln Gln Leu Leu
            740                 745                 750

Pro Leu Gly Asn Ile Ser Asp Asn Val Asp Arg Ile Arg Glu Leu Ile
        755                 760                 765

Thr Gln Ala Arg Asp Ala Ala Asn Lys Val Ala Ile Pro Met Arg Phe
```

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    770                 775                 780

Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu Asp
785                 790                 795                 800

Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asp Leu
                805                 810                 815

Arg Glu Asn Gly Gly Thr Glu Asp Met Phe Val Met Tyr Leu Gly Asn
            820                 825                 830

Lys Asp Ala Ser Lys Asp Tyr Ile Gly Met Ala Val Val Asp Gly Gln
        835                 840                 845

Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Val Gln Ile
    850                 855                 860

Asp Gln Val Leu Thr Glu Ser Glu Ser Gln Glu Ala Val Met Asp Arg
865                 870                 875                 880

Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Lys Leu Asn Tyr Thr Lys
                885                 890                 895

Glu Ala Thr Ser Asn Lys Pro Lys Ala Pro Ala Val Tyr Asp Leu Glu
            900                 905                 910

Gly Gly Ser Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asp Ala Val
        915                 920                 925

Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Glu Leu Pro Ser Arg Leu
    930                 935                 940

Arg Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn Glu
945                 950                 955                 960

Asn Val Leu Ser Leu Tyr Asn Phe Lys Thr Thr Phe Asn Leu Asn Thr
                965                 970                 975

Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys Asn
            980                 985                 990

Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Ile Pro Thr Gln Pro Asn Ala
        995                1000                1005

Pro Phe Pro Asn Phe Ile Gln Thr Ile Gln Thr Thr Val Asp Arg Gly
   1010                1015                1020

Leu Leu Phe Phe Ala Glu Asn Gln Asp Asn Phe Ile Ser Leu Asn Ile
1025                1030                1035                1040

Glu Asp Gly Asn Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Pro Pro
                1045                1050                1055

Lys Glu Lys Gly Ile Arg Asp Thr Ile Asn Asp Gly Lys Asp His Ser
            1060                1065                1070

Ile Leu Ile Thr Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn Val
        1075                1080                1085

Asn Glu Arg Ser Val Arg Ile Glu Gly Glu Ile Phe Asp Phe Ser Thr
   1090                1095                1100
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Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn Ile
1105                1110                1115                1120

Ser Thr Pro Ala Phe Gln Gly Cys Met Lys Asn Leu Lys Lys Thr Ser
                1125                1130                1135

Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys Ser
            1140                1145                1150

Glu Asp Trp Lys Leu Val Arg Thr Ala Ser Phe Ser Arg Gly Gly Gln
        1155                1160                1165

Met Ser Phe Thr Asn Leu Asp Val Pro Ser Thr Asp Arg Phe Gln Leu
    1170                1175                1180

Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Thr Leu Leu Asn His
1185                1190                1195                1200

Gln Thr Arg Thr Ser Ser Leu Leu Val Thr Leu Glu Asp Gly His Ile
                1205                1210                1215

Glu Leu Ser Thr Arg Asp Ser Asn Ile Pro Ile Phe Lys Ser Pro Gly
            1220                1225                1230

Thr Tyr Met Asp Gly Leu Leu His His Val Ser Val Ile Ser Asp Thr
        1235                1240                1245

Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Val Leu Arg Arg Asn Gln
    1250                1255                1260

Arg Leu Pro Ser Phe Ser Asn Ala Gln Gln Ser Leu Arg Leu Gly Gly
1265                1270                1275                1280

Gly His Phe Glu Gly Cys Ile Ser Asn Val Leu Val Gln Arg Phe Ser
                1285                1290                1295

Gln Ser Pro Glu Val Leu Asp Leu Ala Ser Lys Ser Thr Lys Lys Asp
            1300                1305                1310

Ala Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met Leu
        1315                1320                1325

Phe Lys Ser Pro Lys Arg Phe Asn Lys Gly Arg Ile Phe Asn Val Asn
    1330                1335                1340

Gln Leu Met Gln Asp Ala Pro Gln Ala Thr Arg Ser Thr Glu Ala Trp
1345                1350                1355                1360

Gln Asp Gly Arg Ser Cys Leu Pro Pro Leu Asn Thr Lys Ala Ser His
                1365                1370                1375

Arg Ala Leu Gln Phe Gly Asp Ser Pro Thr Ser His Leu Leu Leu Lys
            1380                1385                1390

Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ser Leu Asp Ile
        1395                1400                1405

Gln Thr Thr Ser Pro Lys Gly Leu Val Phe Tyr Ala Gly Thr Lys Asp
    1410                1415                1420
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Ser Phe Leu Ala Leu Tyr Val Ala Asp Gly Arg Val Val Phe Ala Leu
1425 1430 1435 1440

Gly Ala Gly Gly Lys Lys Leu Arg Leu Arg Ser Lys Glu Arg Tyr His
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Asp Gly Lys Trp His Thr Val Val Phe Gly Leu Asn Gly Gly Lys Ala
1460 1465 1470

Arg Leu Val Val Asp Gly Leu Arg Ala Gln Glu Gly Ser Leu Pro Gly
1475 1480 1485

Asn Ser Thr Ile Ser Pro Arg Glu Gln Val Tyr Leu Gly Leu Pro Leu
1490 1495 1500

Ser Arg Lys Pro Lys Ser Leu Pro Gln His Ser Phe Val Gly Cys Leu
1505 1510 1515 1520

Arg Asp Phe Gln Leu Asn Ser Lys Pro Leu Asp Ser Pro Ser Ala Arg
1525 1530 1535

Phe Gly Val Ser Pro Cys Leu Gly Gly Ser Leu Glu Lys Gly Ile Tyr
1540 1545 1550

Phe Ser Gln Gly Gly Gly His Val Ile Leu Ala Asn Ser Val Ser Leu
1555 1560 1565

Gly Pro Glu Leu Lys Leu Thr Phe Ser Ile Arg Pro Arg Ser Leu Thr
1570 1575 1580

Gly Val Leu Ile His Val Gly Ser Gln Ser Gly Gln Arg Leu Ser Val
1585 1590 1595 1600

Tyr Met Glu Ala Gly Lys Val Thr Thr Ser Val Ser Ser Asp Ala Gly
1605 1610 1615

Gly Ser Val Thr Ser Ile Thr Pro Lys Gln Ser Leu Cys Asp Gly Gln
1620 1625 1630

Trp His Ser Val Ala Val Ser Ile Lys Gln Arg Ile Leu His Leu Glu
1635 1640 1645

Leu Asp Thr Asp Ser Ser Tyr Thr Val Ala Pro Leu Ser Phe Ser Pro
1650 1655 1660

Asn Ser Thr Arg Gly Ser Leu His Val Gly Gly Val Pro Asp Lys Leu
1665 1670 1675 1680

Lys Met Leu Thr Leu Pro Val Trp Asn Ser Phe Phe Gly Cys Leu Lys
1685 1690 1695

Asn Ile Gln Val Asn His Val Pro Val Pro Ile Thr Glu Ala Thr Glu
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Val Gln Gly Ser Val Ser Leu Asn Gly Cys Pro Asp His
1715 1720 1725

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  1               5                  10                  15

gca agt tat atg gag ctt aga ccc agc cag ggc tgt cgc cca gga tac   96
Ala Ser Tyr Met Glu Leu Arg Pro Ser Gln Gly Cys Arg Pro Gly Tyr
             20                  25                  30

tat cga gac atc aaa agc ttc cct gcg gga agg tct gtt ccc tgc aat  144
Tyr Arg Asp Ile Lys Ser Phe Pro Ala Gly Arg Ser Val Pro Cys Asn
         35                  40                  45

tgc aac gga cat tca aat aga tgc caa gac ggc tcg gga gtg tgc att  192
Cys Asn Gly His Ser Asn Arg Cys Gln Asp Gly Ser Gly Val Cys Ile
     50                  55                  60

aac tgt cag cac aac aca gct ggg gag cac tgt gag cgt tgc aag agg  240
Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Lys Arg
 65                  70                  75                  80

ggt tac tat gga agc gcc atc cat gga tcc tgc agg gtt tgc ccc tgt  288
Gly Tyr Tyr Gly Ser Ala Ile His Gly Ser Cys Arg Val Cys Pro Cys
                 85                  90                  95

cct cac acc aac agc ttt gcc act ggc tgt gct gtg gat gga gga gct  336
Pro His Thr Asn Ser Phe Ala Thr Gly Cys Ala Val Asp Gly Gly Ala
            100                 105                 110

gtg agg tgt gcc tgc aaa ccc gga tac aca gga gca cag tgt gag agg  384
Val Arg Cys Ala Cys Lys Pro Gly Tyr Thr Gly Ala Gln Cys Glu Arg
        115                 120                 125

tgt gca cca gga tat ttt ggg aac ccc cag aaa ttt gga ggt agc tgc  432
Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys
    130                 135                 140

caa cca tgc aat tgc aac agt aat ggc cag ttt ggc act tgt gat ccc  480
Gln Pro Cys Asn Cys Asn Ser Asn Gly Gln Phe Gly Thr Cys Asp Pro
145                 150                 155                 160

cta act gga gac tgt gta agc caa gaa ccc aaa gat ggc agc cct gca  528
Leu Thr Gly Asp Cys Val Ser Gln Glu Pro Lys Asp Gly Ser Pro Ala
                165                 170                 175

gaa gaa tgt gat gac tgt gac agc tgt gtg atg act ctc cta aat gac  576
Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp
            180                 185                 190

ttg gtc ccc atg ggt gag gaa ctc gcc ctg gtg aaa tca aaa ctt cag  624
Leu Val Pro Met Gly Glu Glu Leu Ala Leu Val Lys Ser Lys Leu Gln
        195                 200                 205

ggg ctg agt gtg aac act ggt tct ctg gaa cag atc cgg cat gtg gag  672
Gly Leu Ser Val Asn Thr Gly Ser Leu Glu Gln Ile Arg His Val Glu
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atg cag gcc aag gac ctg agg aac cag ctg ctt ggc ttc cgt tcc gcc   720
Met Gln Ala Lys Asp L u Arg Asn Gln Leu Leu Gly Phe Arg Ser Ala
225                 230                 235                 240

atc tcc agt cac ggg tcc caa atg gac ggc ctg gaa aaa gaa ctc agt   768
Ile Ser Ser His Gly Ser Gln Met Asp Gly Leu Glu Lys Glu Leu Ser
                245                 250                 255

cat ttg tac cag gaa ttc gaa act ttg caa gaa aag gcg cag gtc aat   816
His Leu Tyr Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn
            260                 265                 270

tcc aga aaa gca caa aca tta tat aac aac atc gat acg aca atc caa   864
Ser Arg Lys Ala Gln Thr Leu Tyr Asn Asn Ile Asp Thr Thr Ile Gln
        275                 280                 285

aac gcc aaa gag ttg gac atg aag att aaa aac ata ctt acg aat gtg   912
Asn Ala Lys Glu Leu Asp Met Lys Ile Lys Asn Ile Leu Thr Asn Val
    290                 295                 300

cac att ctc ctg aag cag atc gct cgg cca ggt gga gaa gga atg gac   960
His Ile Leu Leu Lys Gln Ile Ala Arg Pro Gly Gly Glu Gly Met Asp
305                 310                 315                 320

ttg ccg gtg ggc gac tgg tcc agg gag tcg gcg gaa gct cag cgc atg   1008
Leu Pro Val Gly Asp Trp Ser Arg Glu Ser Ala Glu Ala Gln Arg Met
                325                 330                 335

ttg cgg gag ctg cga ggc cga gac ttt aaa aag cac ctc caa gaa gca   1056
Leu Arg Glu Leu Arg Gly Arg Asp Phe Lys Lys His Leu Gln Glu Ala
            340                 345                 350

gag gcc cag aaa atg gaa gcc cag ctc tta ctg aac cga atc agg acc   1104
Glu Ala Gln Lys Met Glu Ala Gln Leu Leu Leu Asn Arg Ile Arg Thr
        355                 360                 365

tgg ctg gaa tcc cac cag gtg gag aac aat gga ctg cta aag aat att   1152
Trp Leu Glu Ser His Gln Val Glu Asn Asn Gly Leu Leu Lys Asn Ile
    370                 375                 380

cgg gat tca tta aat gat tat gaa gcc aaa ctt cag gac ctg cgt tcc   1200
Arg Asp Ser Leu Asn Asp Tyr Glu Ala Lys Leu Gln Asp Leu Arg Ser
385                 390                 395                 400

gtg ctt cag gag gcg gca gcc cag gga aag cag gct aca ggc ctc aac   1248
Val Leu Gln Glu Ala Ala Ala Gln Gly Lys Gln Ala Thr Gly Leu Asn
                405                 410                 415

cac gaa aat gag ggg gtc cta gga gcc atc cag aga caa atg aag gaa   1296
His Glu Asn Glu Gly Val Leu Gly Ala Ile Gln Arg Gln Met Lys Glu
            420                 425                 430

atg gat tcc ctg aag aag tac ctc acc gag cac ctg gcc aca gca gac   1344
Met Asp Ser Leu Lys Lys Tyr Leu Thr Glu His Leu Ala Thr Ala Asp
        435                 440                 445

gct tcc ctg ctg caa acc aac agt cta ctg cag cgg atg gac acg agc   1392
Ala Ser Leu Leu Gln Thr Asn Ser Leu Leu Gln Arg Met Asp Thr S r
    450                 455                 460
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cag aag gag tat gaa agc tta gct gct gct tta aac gga gca aga cag   1440
Gln Lys Glu Tyr Glu Ser Leu Ala Ala Ala Leu Asn Gly Ala Arg Gln
465                 470                 475                 480

gaa ctg aat gac caa gtg cgg gaa ctc tcc aga tcc gga ggc aaa gca   1488
Glu Leu Asn Asp Gln Val Arg Glu Leu Ser Arg Ser Gly Gly Lys Ala
                485                 490                 495

ccc ctg gtg gct gag gcc gag aag cac gct cag tct tta cag gag ctg   1536
Pro Leu Val Ala Glu Ala Glu Lys His Ala Gln Ser Leu Gln Glu Leu
            500                 505                 510

gca aag cag ctg gaa gag ata aag aga aac acc agt ggg gat gag tcg   1584
Ala Lys Gln Leu Glu Glu Ile Lys Arg Asn Thr Ser Gly Asp Glu Ser
        515                 520                 525

gtg cgc tgt gtc gtg gac gct gcc act gcc tat gag agc atc ctc aac   1632
Val Arg Cys Val Val Asp Ala Ala Thr Ala Tyr Glu Ser Ile Leu Asn
    530                 535                 540

gcc atc cga gca gca gag gat gca gcc ggc aag gcc gac agt gcc tca   1680
Ala Ile Arg Ala Ala Glu Asp Ala Ala Gly Lys Ala Asp Ser Ala Ser
545                 550                 555                 560

gag tcc gcc ttc cag aca gtg ata aag gaa gat ctt ccg aga aga gcc   1728
Glu Ser Ala Phe Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Arg Ala
                565                 570                 575

aaa acc ctg agt tct gac agc gag gaa ctg tta aac gag gcc aag atg   1776
Lys Thr Leu Ser Ser Asp Ser Glu Glu Leu Leu Asn Glu Ala Lys Met
            580                 585                 590

aca cgg aaa agg cta cag caa gaa atc aat cca gct ctc aac agc cta   1824
Thr Arg Lys Arg Leu Gln Gln Glu Ile Asn Pro Ala Leu Asn Ser Leu
        595                 600                 605

cag caa acc ctg aag act gta tca gtt cag aag gac ctg cta gat gcc   1872
Gln Gln Thr Leu Lys Thr Val Ser Val Gln Lys Asp Leu Leu Asp Ala
    610                 615                 620

aat gtc act gct gtc cgt aat gac ctt cgt ggg atc cag aga ggt gat   1920
Asn Val Thr Ala Val Arg Asn Asp Leu Arg Gly Ile Gln Arg Gly Asp
625                 630                 635                 640

att gac agt gtg gtg agt gga gcg aag agc atg gtc agg aaa gcc aat   1968
Ile Asp Ser Val Val Ser Gly Ala Lys Ser Met Val Arg Lys Ala Asn
                645                 650                 655

ggg ata acg agc gag gtc ctg gac ggg ctc agc ccc atc cag acg gat   2016
Gly Ile Thr Ser Glu Val Leu Asp Gly Leu Ser Pro Ile Gln Thr Asp
            660                 665                 670

ttg gga agg att aag gac agc tac ggg agc aca cgg cat gag gac ttc   2064
Leu Gly Arg Ile Lys Asp Ser Tyr Gly Ser Thr Arg His Glu Asp Phe
        675                 680                 685

aac aaa gct ctg att gac gcc aat aac tca gta aag aaa tta acc aag   2112
Asn Lys Ala Leu Ile Asp Ala Asn Asn Ser Val Lys Lys Leu Thr Lys
    690                 695                 700
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aag ttg cct gat ctt ttt gtc aag att gaa agc atc aat caa cag ttg   2160
Lys Leu Pro Asp Leu Phe Val Lys Ile Glu Ser Ile Asn Gln Gln Leu
705                 710                 715                 720

ctg ccc ctg gga aac atc tct gac aat gta gac cga atc cga gag ctc   2208
Leu Pro Leu Gly Asn Ile Ser Asp Asn Val Asp Arg Ile Arg Glu Leu
                725                 730                 735

att acg cag gcc aga gat gct gcg aac aag gtt gca att ccc atg agg   2256
Ile Thr Gln Ala Arg Asp Ala Ala Asn Lys Val Ala Ile Pro Met Arg
            740                 745                 750

ttc aat ggt aaa tct ggt gtt gaa gtc cgt ctg cca aat gac cta gaa   2304
Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu
        755                 760                 765

gac ttg aag gga tac acg tct ctg tct ttg ttc ctc caa aga cca gac   2352
Asp Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asp
    770                 775                 780

tta aga gag aat gga ggc act gag gac atg ttt gta atg tac ctt gga   2400
Leu Arg Glu Asn Gly Gly Thr Glu Asp Met Phe Val Met Tyr Leu Gly
785                 790                 795                 800

aac aag gat gcc tcc aag gac tac atc ggc atg gcg gtt gta gat ggc   2448
Asn Lys Asp Ala Ser Lys Asp Tyr Ile Gly Met Ala Val Val Asp Gly
                805                 810                 815

cag ctg acg tgt gtc tac aac ctg ggg gac cga gaa gct gaa gtt cag   2496
Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Val Gln
            820                 825                 830

atc gat cag gtc ctg acg gag agt gag tct cag gag gca gtt atg gac   2544
Ile Asp Gln Val Leu Thr Glu Ser Glu Ser Gln Glu Ala Val Met Asp
        835                 840                 845

cgg gtg aag ttc cag aga ata tat caa ttt gcc aag ctt aat tac acc   2592
Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Lys Leu Asn Tyr Thr
    850                 855                 860

aaa gaa gcc acg tcc aat aaa ccc aaa gct ccc gcg gtc tac gac ctg   2640
Lys Glu Ala Thr Ser Asn Lys Pro Lys Ala Pro Ala Val Tyr Asp Leu
865                 870                 875                 880

gag ggt ggc agt agc aac acg ctc ctt aat ttg gat ccc gag gac gct   2688
Glu Gly Gly Ser Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asp Ala
                885                 890                 895

gtg ttt tat gtc gga ggt tac cca ccg gat ttt gaa ctt cct agc aga   2736
Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Glu Leu Pro Ser Arg
            900                 905                 910

ctg cgg ttc cct cca tac aaa ggc tgt atc gaa cta gat gac ctc aat   2784
Leu Arg Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn
        915                 920                 925

gaa aac gtt cta agc ttg tac aat ttc aag aca act ttc aat ctc aac   2832
Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Thr Thr Phe Asn Leu Asn
    930                 935                 940

acc acg gag gtg gag cct tgt agg agg aga aag gaa gag tca gac aaa   2880
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Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys
945                 950                 955                 960

aat tac ttt gaa ggt aca ggc tat gct cgc atc cct act caa cca aat   2928
Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Ile Pro Thr Gln Pro Asn
                965                 970                 975

gct ccc ttc cca aac ttc ata cag acc atc cag act act gtg gac aga   2976
Ala Pro Phe Pro Asn Phe Ile Gln Thr Ile Gln Thr Thr Val Asp Arg
            980                 985                 990

ggt tta ctg ttc ttc gca gaa aac cag gat aac ttc ata tct ctg aac   3024
Gly Leu Leu Phe Phe Ala Glu Asn Gln Asp Asn Phe Ile Ser Leu Asn
        995                1000                1005

ata gaa gat ggc aat ctc atg gtg aga tac aaa cta aat tca gag cca   3072
Ile Glu Asp Gly Asn Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Pro
   1010                1015                1020

ccc aaa gag aag gga att cga gac acc atc aac gat ggg aaa gat cat   3120
Pro Lys Glu Lys Gly Ile Arg Asp Thr Ile Asn Asp Gly Lys Asp His
1025                1030                1035                1040

tcg atc tta atc aca att gga aaa cta caa aaa cgc atg tgg ata aat   3168
Ser Ile Leu Ile Thr Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn
                1045                1050                1055

gtg aac gaa cgc agt gta cga atc gaa ggg gaa ata ttt gat ttc agc   3216
Val Asn Glu Arg Ser Val Arg Ile Glu Gly Glu Ile Phe Asp Phe Ser
            1060                1065                1070

aca tat tat ttg ggc gga att cca att gca atc aga gaa agg ttt aac   3264
Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn
        1075                1080                1085

atc tca acg cct gct ttc caa ggc tgc atg aag aat ctg aag aaa acc   3312
Ile Ser Thr Pro Ala Phe Gln Gly Cys Met Lys Asn Leu Lys Lys Thr
   1090                1095                1100

agt ggg gtt gtc agg ttg aat gat act gtg ggt gta acc aag aag tgc   3360
Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys
1105                1110                1115                1120

tca gaa gac tgg aag ctt gtg cga acc gcc tcg ttc tcc aga gga ggg   3408
Ser Glu Asp Trp Lys Leu Val Arg Thr Ala Ser Phe Ser Arg Gly Gly
                1125                1130                1135

cag atg agc ttt aca aac ttg gac gtg ccc tcg act gac cgc ttc cag   3456
Gln Met Ser Phe Thr Asn Leu Asp Val Pro Ser Thr Asp Arg Phe Gln
            1140                1145                1150

ctc tcc ttt ggg ttt cag acc ttt caa ccc agt ggc aca ctg ctc aat   3504
Leu Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Thr Leu Leu Asn
        1155                1160                1165

cat cag acg cgg aca agc agc ctg ctg gtc acc ctg gaa gat ggg cac   3552
His Gln Thr Arg Thr Ser Ser Leu Leu Val Thr Leu Glu Asp Gly His
   1170                1175                1180

att gag ttg agc act agg gac agc aac atc cca att ttc aag tct cca   3600
Ile Glu Leu Ser Thr Arg Asp Ser Asn Ile Pro Ile Phe Lys Ser Pro
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1185                1190                1195                1200

ggg acc tac atg gac ggt tta ctg cat cat gta tct gta ata agt gac   3648
Gly Thr Tyr Met Asp Gly Leu Leu His His Val Ser Val Ile Ser Asp
                1205                1210                1215

acc tca ggt ctc cgc ctt ctc atc gat gac cag gtc ctg aga agg aac   3696
Thr Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Val Leu Arg Arg Asn
            1220                1225                1230

cag agg ctt cct agc ttc tct aac gcc cag cag tcg ctc cgc ctt gga   3744
Gln Arg Leu Pro Ser Phe Ser Asn Ala Gln Gln Ser Leu Arg Leu Gly
        1235                1240                1245

gga ggt cat ttc gag ggt tgt atc agc aat gtt tta gtc caa agg ttt   3792
Gly Gly His Phe Glu Gly Cys Ile Ser Asn Val Leu Val Gln Arg Phe
    1250                1255                1260

tca cag agt cca gaa gtc ctg gat ctg gcc agt aaa tct acc aag aag   3840
Ser Gln Ser Pro Glu Val Leu Asp Leu Ala Ser Lys Ser Thr Lys Lys
1265                1270                1275                1280

gat gca tcc cta gga ggc tgc agt tta aac aag cca cct ttt ctt atg   3888
Asp Ala Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met
                1285                1290                1295

ttg ttt aaa agt ccc aag aga ttt aac aag ggc cgg att ttc aat gtt   3936
Leu Phe Lys Ser Pro Lys Arg Phe Asn Lys Gly Arg Ile Phe Asn Val
            1300                1305                1310

aat cag ctg atg caa gat gca cct cag gcc aca agg agc aca gag gct   3984
Asn Gln Leu Met Gln Asp Ala Pro Gln Ala Thr Arg Ser Thr Glu Ala
        1315                1320                1325

tgg caa gat ggg agg tcc tgc cta cca cct ctg aac acc aag gcc tct   4032
Trp Gln Asp Gly Arg Ser Cys Leu Pro Pro Leu Asn Thr Lys Ala Ser
    1330                1335                1340

cac aga gcc ctg cag ttt gga gac agc ccc acc agc cac ttg cta ctc   4080
His Arg Ala Leu Gln Phe Gly Asp Ser Pro Thr Ser His Leu Leu Leu
1345                1350                1355                1360

aag ctt ccc cag gaa ctg ctg aaa cct agg tca cag ttt tct tta gac   4128
Lys Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ser Leu Asp
                1365                1370                1375

ata cag aca act tcc ccc aaa gga ctg gtg ttt tac gca ggc acc aag   4176
Ile Gln Thr Thr Ser Pro Lys Gly Leu Val Phe Tyr Ala Gly Thr Lys
            1380                1385                1390

gac tcc ttc ctg gct ctt tat gtc gca gat ggc cgt gtt gtc ttt gct   4224
Asp Ser Phe Leu Ala Leu Tyr Val Ala Asp Gly Arg Val Val Phe Ala
        1395                1400                1405

ttg ggg gca gga ggg aag aaa ctg aga ctc agg agc aag gag aga tac   4272
Leu Gly Ala Gly Gly Lys Lys Leu Arg Leu Arg Ser Lys Glu Arg Tyr
    1410                1415                1420

cat gac ggg aag tgg cac acg gtg gtg ttc gga cta aat gga gga aag   4320
His Asp Gly Lys Trp His Thr Val Val Phe Gly Leu Asn Gly Gly Lys
1425                1430                1435                1440
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gca cgc ctg gtt gtg gat ggg cta agg gcc cag gaa ggc agt ttg cct   4368
Ala Arg Leu Val Val Asp Gly Leu Arg Ala Gln Glu Gly Ser Leu Pro
               1445                1450                1455

gga aat tct acc atc agc ccc aga gaa cag gtt tac cta ggg ttg ccg   4416
Gly Asn Ser Thr Ile Ser Pro Arg Glu Gln Val Tyr Leu Gly Leu Pro
           1460                1465                1470

cta tca aga aag cca aag agc cta ccc cag cac agt ttt gtg ggg tgc   4464
Leu Ser Arg Lys Pro Lys Ser Leu Pro Gln His Ser Phe Val Gly Cys
       1475                1480                1485

ctg aga gat ttc cag ttg aac tcg aaa ccc ctg gat tct cct tct gcg   4512
Leu Arg Asp Phe Gln Leu Asn Ser Lys Pro Leu Asp Ser Pro Ser Ala
   1490                1495                1500

agg ttt ggg gta tct ccc tgc ttg ggt ggc tct tta gag aaa ggc att   4560
Arg Phe Gly Val Ser Pro Cys Leu Gly Gly Ser Leu Glu Lys Gly Ile
1505                1510                1515                1520

tat ttc tcc caa gga gga ggc cat gtg atc cta gcc aat tct gtg tcc   4608
Tyr Phe Ser Gln Gly Gly Gly His Val Ile Leu Ala Asn Ser Val Ser
               1525                1530                1535

ttg ggg cca gag ctt aag ctc act ttc agc att cgc cca cgg agt ctc   4656
Leu Gly Pro Glu Leu Lys Leu Thr Phe Ser Ile Arg Pro Arg Ser Leu
           1540                1545                1550

act ggg gtc tta ata cac gtc gga agt caa tct gga cag cgc tta agt   4704
Thr Gly Val Leu Ile His Val Gly Ser Gln Ser Gly Gln Arg Leu Ser
       1555                1560                1565

gtg tac atg gag gca gga aag gtc aca acc tct gtg agc agt gat gca   4752
Val Tyr Met Glu Ala Gly Lys Val Thr Thr Ser Val Ser Ser Asp Ala
   1570                1575                1580

gga gga agt gtg aca tca att aca ccg aag cag tct ctg tgt gat gga   4800
Gly Gly Ser Val Thr Ser Ile Thr Pro Lys Gln Ser Leu Cys Asp Gly
1585                1590                1595                1600

cag tgg cac tcg gtg gca gtc tcc att aaa cag cgc atc ctg cat cta   4848
Gln Trp His Ser Val Ala Val Ser Ile Lys Gln Arg Ile Leu His Leu
               1605                1610                1615

gaa ctg gat aca gac agt agc tac aca gtc gca cca ctt tcc ttc tca   4896
Glu Leu Asp Thr Asp Ser Ser Tyr Thr Val Ala Pro Leu Ser Phe Ser
           1620                1625                1630

cca aac agc acc cga ggg tca ctg cac gtc gga ggt gtc cca gac aaa   4944
Pro Asn Ser Thr Arg Gly Ser Leu His Val Gly Gly Val Pro Asp Lys
       1635                1640                1645

ttg aaa atg ctt aca ctc cct gtg tgg aac tca ttt ttt ggc tgt ctg   4992
Leu Lys Met Leu Thr Leu Pro Val Trp Asn Ser Phe Phe Gly Cys Leu
   1650                1655                1660

aag aat att caa gtc aac cat gtc cct gtc ccc atc aca gaa gcc aca   5040
Lys Asn Ile Gln Val Asn His Val Pro Val Pro Ile Thr Glu Ala Thr
1665                1670                1675                1680
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gaa gtc caa ggt tct gtc agc ctg aat ggc tgc cct gac cac          5082
Glu Val Gln Gly Ser Val Ser Leu Asn Gly Cys Pro Asp His
               1685                1690

taaccctaca cagcaagatt caccttgga g                                5113


<210> 12
<211> 1694
<212> PRT
<213> Rattus norvegicus

<400> 12
Gln Gln Arg Val Ala Phe Leu Gln His Pro Gly Gln Asn His Leu Gln
  1               5                  10                  15

Ala Ser Tyr Met Glu Leu Arg Pro Ser Gln Gly Cys Arg Pro Gly Tyr
             20                  25                  30

Tyr Arg Asp Ile Lys Ser Phe Pro Ala Gly Arg Ser Val Pro Cys Asn
         35                  40                  45

Cys Asn Gly His Ser Asn Arg Cys Gln Asp Gly Ser Gly Val Cys Ile
     50                  55                  60

Asn Cys Gln His Asn Thr Ala Gly Glu His Cys Glu Arg Cys Lys Arg
 65                  70                  75                  80

Gly Tyr Tyr Gly Ser Ala Ile His Gly Ser Cys Arg Val Cys Pro Cys
                 85                  90                  95

Pro His Thr Asn Ser Phe Ala Thr Gly Cys Ala Val Asp Gly Gly Ala
            100                 105                 110

Val Arg Cys Ala Cys Lys Pro Gly Tyr Thr Gly Ala Gln Cys Glu Arg
        115                 120                 125

Cys Ala Pro Gly Tyr Phe Gly Asn Pro Gln Lys Phe Gly Gly Ser Cys
    130                 135                 140

Gln Pro Cys Asn Cys Asn Ser Asn Gly Gln Phe Gly Thr Cys Asp Pro
145                 150                 155                 160

Leu Thr Gly Asp Cys Val Ser Gln Glu Pro Lys Asp Gly Ser Pro Ala
                165                 170                 175

Glu Glu Cys Asp Asp Cys Asp Ser Cys Val Met Thr Leu Leu Asn Asp
            180                 185                 190

Leu Val Pro Met Gly Glu Glu Leu Ala Leu Val Lys Ser Lys Leu Gln
        195                 200                 205

Gly Leu Ser Val Asn Thr Gly Ser Leu Glu Gln Ile Arg His Val Glu
    210                 215                 220

Met Gln Ala Lys Asp Leu Arg Asn Gln Leu Leu Gly Phe Arg Ser Ala
225                 230                 235                 240

Ile Ser Ser His Gly Ser Gln Met Asp Gly Leu Glu Lys Glu Leu Ser
                245                 250                 255
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His Leu Tyr Gln Glu Phe Glu Thr Leu Gln Glu Lys Ala Gln Val Asn
260 265 270

Ser Arg Lys Ala Gln Thr Leu Tyr Asn Asn Ile Asp Thr Thr Ile Gln
275 280 285

Asn Ala Lys Glu Leu Asp Met Lys Ile Lys Asn Ile Leu Thr Asn Val
290 295 300

His Ile Leu Leu Lys Gln Ile Ala Arg Pro Gly Gly Glu Gly Met Asp
305 310 315 320

Leu Pro Val Gly Asp Trp Ser Arg Glu Ser Ala Glu Ala Gln Arg Met
325 330 335

Leu Arg Glu Leu Arg Gly Arg Asp Phe Lys Lys His Leu Gln Glu Ala
340 345 350

Glu Ala Gln Lys Met Glu Ala Gln Leu Leu Leu Asn Arg Ile Arg Thr
355 360 365

Trp Leu Glu Ser His Gln Val Glu Asn Asn Gly Leu Leu Lys Asn Ile
370 375 380

Arg Asp Ser Leu Asn Asp Tyr Glu Ala Lys Leu Gln Asp Leu Arg Ser
385 390 395 400

Val Leu Gln Glu Ala Ala Ala Gln Gly Lys Gln Ala Thr Gly Leu Asn
405 410 415

His Glu Asn Glu Gly Val Leu Gly Ala Ile Gln Arg Gln Met Lys Glu
420 425 430

Met Asp Ser Leu Lys Lys Tyr Leu Thr Glu His Leu Ala Thr Ala Asp
435 440 445

Ala Ser Leu Leu Gln Thr Asn Ser Leu Leu Gln Arg Met Asp Thr Ser
450 455 460

Gln Lys Glu Tyr Glu Ser Leu Ala Ala Ala Leu Asn Gly Ala Arg Gln
465 470 475 480

Glu Leu Asn Asp Gln Val Arg Glu Leu Ser Arg Ser Gly Gly Lys Ala
485 490 495

Pro Leu Val Ala Glu Ala Glu Lys His Ala Gln Ser Leu Gln Glu Leu
500 505 510

Ala Lys Gln Leu Glu Glu Ile Lys Arg Asn Thr Ser Gly Asp Glu Ser
515 520 525

Val Arg Cys Val Val Asp Ala Ala Thr Ala Tyr Glu Ser Ile Leu Asn
530 535 540

Ala Ile Arg Ala Ala Glu Asp Ala Ala Gly Lys Ala Asp Ser Ala Ser
545 550 555 560

Glu Ser Ala Phe Gln Thr Val Ile Lys Glu Asp Leu Pro Arg Arg Ala
565 570 575

Lys Thr Leu Ser Ser Asp Ser Glu Glu Leu Leu Asn Glu Ala Lys Met

580 585 590

Thr Arg Lys Arg Leu Gln Gln Glu Ile Asn Pro Ala Leu Asn Ser Leu
595 600 605

Gln Gln Thr Leu Lys Thr Val Ser Val Gln Lys Asp Leu Leu Asp Ala
610 615 620

Asn Val Thr Ala Val Arg Asn Asp Leu Arg Gly Ile Gln Arg Gly Asp
625 630 635 640

Ile Asp Ser Val Val Ser Gly Ala Lys Ser Met Val Arg Lys Ala Asn
645 650 655

Gly Ile Thr Ser Glu Val Leu Asp Gly Leu Ser Pro Ile Gln Thr Asp
660 665 670

Leu Gly Arg Ile Lys Asp Ser Tyr Gly Ser Thr Arg His Glu Asp Phe
675 680 685

Asn Lys Ala Leu Ile Asp Ala Asn Asn Ser Val Lys Lys Leu Thr Lys
690 695 700

Lys Leu Pro Asp Leu Phe Val Lys Ile Glu Ser Ile Asn Gln Gln Leu
705 710 715 720

Leu Pro Leu Gly Asn Ile Ser Asp Asn Val Asp Arg Ile Arg Glu Leu
725 730 735

Ile Thr Gln Ala Arg Asp Ala Ala Asn Lys Val Ala Ile Pro Met Arg
740 745 750

Phe Asn Gly Lys Ser Gly Val Glu Val Arg Leu Pro Asn Asp Leu Glu
755 760 765

Asp Leu Lys Gly Tyr Thr Ser Leu Ser Leu Phe Leu Gln Arg Pro Asp
770 775 780

Leu Arg Glu Asn Gly Gly Thr Glu Asp Met Phe Val Met Tyr Leu Gly
785 790 795 800

Asn Lys Asp Ala Ser Lys Asp Tyr Ile Gly Met Ala Val Val Asp Gly
805 810 815

Gln Leu Thr Cys Val Tyr Asn Leu Gly Asp Arg Glu Ala Glu Val Gln
820 825 830

Ile Asp Gln Val Leu Thr Glu Ser Glu Ser Gln Glu Ala Val Met Asp
835 840 845

Arg Val Lys Phe Gln Arg Ile Tyr Gln Phe Ala Lys Leu Asn Tyr Thr
850 855 860

Lys Glu Ala Thr Ser Asn Lys Pro Lys Ala Pro Ala Val Tyr Asp Leu
865 870 875 880

Glu Gly Gly Ser Ser Asn Thr Leu Leu Asn Leu Asp Pro Glu Asp Ala
885 890 895

Val Phe Tyr Val Gly Gly Tyr Pro Pro Asp Phe Glu Leu Pro Ser Arg
900 905 910

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Leu Arg Phe Pro Pro Tyr Lys Gly Cys Ile Glu Leu Asp Asp Leu Asn
        915                 920                 925

Glu Asn Val Leu Ser Leu Tyr Asn Phe Lys Thr Thr Phe Asn Leu Asn
    930                 935                 940

Thr Thr Glu Val Glu Pro Cys Arg Arg Arg Lys Glu Glu Ser Asp Lys
945                 950                 955                 960

Asn Tyr Phe Glu Gly Thr Gly Tyr Ala Arg Ile Pro Thr Gln Pro Asn
                965                 970                 975

Ala Pro Phe Pro Asn Phe Ile Gln Thr Ile Gln Thr Thr Val Asp Arg
            980                 985                 990

Gly Leu Leu Phe Phe Ala Glu Asn Gln Asp Asn Phe Ile Ser Leu Asn
        995                1000                1005

Ile Glu Asp Gly Asn Leu Met Val Arg Tyr Lys Leu Asn Ser Glu Pro
   1010                1015                1020

Pro Lys Glu Lys Gly Ile Arg Asp Thr Ile Asn Asp Gly Lys Asp His
1025                1030                1035                1040

Ser Ile Leu Ile Thr Ile Gly Lys Leu Gln Lys Arg Met Trp Ile Asn
                1045                1050                1055

Val Asn Glu Arg Ser Val Arg Ile Glu Gly Glu Ile Phe Asp Phe Ser
            1060                1065                1070

Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg Phe Asn
        1075                1080                1085

Ile Ser Thr Pro Ala Phe Gln Gly Cys Met Lys Asn Leu Lys Lys Thr
   1090                1095                1100

Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys Lys Cys
1105                1110                1115                1120

Ser Glu Asp Trp Lys Leu Val Arg Thr Ala Ser Phe Ser Arg Gly Gly
                1125                1130                1135

Gln Met Ser Phe Thr Asn Leu Asp Val Pro Ser Thr Asp Arg Phe Gln
            1140                1145                1150

Leu Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Thr Leu Leu Asn
        1155                1160                1165

His Gln Thr Arg Thr Ser Ser Leu Leu Val Thr Leu Glu Asp Gly His
   1170                1175                1180

Ile Glu Leu Ser Thr Arg Asp Ser Asn Ile Pro Ile Phe Lys Ser Pro
1185                1190                1195                1200

Gly Thr Tyr Met Asp Gly Leu Leu His His Val Ser Val Ile Ser Asp
                1205                1210                1215

Thr Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Val Leu Arg Arg Asn
            1220                1225                1230
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Gln Arg Leu Pro Ser Phe Ser Asn Ala Gln Gln Ser Leu Arg Leu Gly
1235 1240 1245

Gly Gly His Phe Glu Gly Cys Ile Ser Asn Val Leu Val Gln Arg Phe
1250 1255 1260

Ser Gln Ser Pro Glu Val Leu Asp Leu Ala Ser Lys Ser Thr Lys Lys
1265 1270 1275 1280

Asp Ala Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met
1285 1290 1295

Leu Phe Lys Ser Pro Lys Arg Phe Asn Lys Gly Arg Ile Phe Asn Val
1300 1305 1310

Asn Gln Leu Met Gln Asp Ala Pro Gln Ala Thr Arg Ser Thr Glu Ala
1315 1320 1325

Trp Gln Asp Gly Arg Ser Cys Leu Pro Pro Leu Asn Thr Lys Ala Ser
1330 1335 1340

His Arg Ala Leu Gln Phe Gly Asp Ser Pro Thr Ser His Leu Leu Leu
1345 1350 1355 1360

Lys Leu Pro Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ser Leu Asp
1365 1370 1375

Ile Gln Thr Thr Ser Pro Lys Gly Leu Val Phe Tyr Ala Gly Thr Lys
1380 1385 1390

Asp Ser Phe Leu Ala Leu Tyr Val Ala Asp Gly Arg Val Val Phe Ala
1395 1400 1405

Leu Gly Ala Gly Gly Lys Lys Leu Arg Leu Arg Ser Lys Glu Arg Tyr
1410 1415 1420

His Asp Gly Lys Trp His Thr Val Val Phe Gly Leu Asn Gly Gly Lys
1425 1430 1435 1440

Ala Arg Leu Val Val Asp Gly Leu Arg Ala Gln Glu Gly Ser Leu Pro
1445 1450 1455

Gly Asn Ser Thr Ile Ser Pro Arg Glu Gln Val Tyr Leu Gly Leu Pro
1460 1465 1470

Leu Ser Arg Lys Pro Lys Ser Leu Pro Gln His Ser Phe Val Gly Cys
1475 1480 1485

Leu Arg Asp Phe Gln Leu Asn Ser Lys Pro Leu Asp Ser Pro Ser Ala
1490 1495 1500

Arg Phe Gly Val Ser Pro Cys Leu Gly Gly Ser Leu Glu Lys Gly Ile
1505 1510 1515 1520

Tyr Phe Ser Gln Gly Gly Gly His Val Ile Leu Ala Asn Ser Val Ser
1525 1530 1535

Leu Gly Pro Glu Leu Lys Leu Thr Phe Ser Ile Arg Pro Arg Ser Leu
1540 1545 1550

Thr Gly Val Leu Ile His Val Gly Ser Gln Ser Gly Gln Arg Leu Ser

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      1555                1560                1565

Val Tyr Met Glu Ala Gly Lys Val Thr Thr Ser Val Ser Ser Asp Ala
   1570                1575                1580

Gly Gly Ser Val Thr Ser Ile Thr Pro Lys Gln Ser Leu Cys Asp Gly
1585                1590                1595                1600

Gln Trp His Ser Val Ala Val Ser Ile Lys Gln Arg Ile Leu His Leu
               1605                1610                1615

Glu Leu Asp Thr Asp Ser Ser Tyr Thr Val Ala Pro Leu Ser Phe Ser
           1620                1625                1630

Pro Asn Ser Thr Arg Gly Ser Leu His Val Gly Gly Val Pro Asp Lys
       1635                1640                1645

Leu Lys Met Leu Thr Leu Pro Val Trp Asn Ser Phe Phe Gly Cys Leu
   1650                1655                1660

Lys Asn Ile Gln Val Asn His Val Pro Val Pro Ile Thr Glu Ala Thr
1665                1670                1675                1680

Glu Val Gln Gly Ser Val Ser Leu Asn Gly Cys Pro Asp His
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cctcttcctg ggagctcact caggaaaggt cctttctggg gatcacccca ttggctgaag 120

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atg aga cca ttc ttc ctc ttg tgt ttt gcc ctg cct ggc ctc ctg cat   168
Met Arg Pro Phe Phe Leu Leu Cys Phe Ala Leu Pro Gly Leu Leu His
  1               5                  10                  15

gcc caa caa gcc tgc tcc cgt ggg gcc tgc tat cca cct gtt ggg gac   216
Ala Gln Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp
             20                  25                  30

ctg ctt gtt ggg agg acc cgg ttt ctc cga gct tca tct acc tgt gga   264
Leu Leu Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly
         35                  40                  45

ctg acc aag cct gag acc tac tgc acc cag tat ggc gag tgg cag atg   312
Leu Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met
     50                  55                  60
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aaa tgc tgc aag tgt gac tcc agg cag cct cac aac tac tac agt cac   360
Lys Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His
 65                  70                  75                  80

cga gta gag aat gtg gct tca tcc tcc ggc ccc atg cgc tgg tgg cag   408
Arg Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln
                85                  90                  95

tcc cag aat gat gtg aac cct gtc tct ctg cag ctg gac ctg gac agg   456
Ser Gln Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg
            100                 105                 110

aga ttc cag ctt caa gaa gtc atg atg gag ttc cga ggg ccc atg cct   504
Arg Phe Gln Leu Gln Glu Val Met Met Glu Phe Arg Gly Pro Met Pro
        115                 120                 125

gcc ggc atg ctg att gag cgc tcc tca gac ttc ggt aag acc tgg cga   552
Ala Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg
    130                 135                 140

gtg tac cag tac ctg gct gcc gac tgc acc tcc acc ttc cct cgg gtc   600
Val Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val
145                 150                 155                 160

cgc cag ggt cgg cct cag agc tgg cag gat gtt cgg tgc cag tcc ctg   648
Arg Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu
                165                 170                 175

cct cag agg cct aat gca cgc cta aat ggg ggg aag gtc caa ctt aac   696
Pro Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn
            180                 185                 190

ctt atg gat tta gtg tct ggg att cca gca act caa agt caa aaa att   744
Leu Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile
        195                 200                 205

caa gag gtg ggg gag atc aca aac ttg aga gtc aat ttc acc agg ctg   792
Gln Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu
    210                 215                 220

gcc cct gtg ccc caa agg ggc tac cac cct ccc agc gcc tac tat gct   840
Ala Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala
225                 230                 235                 240

gtg tcc cag ctc cgt ctg cag ggg agc tgc ttc tgt cac ggc cat gct   888
Val Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala
                245                 250                 255

gat cgc tgc gca ccc aag cct ggg gcc tct gca ggc tcc acc gct gtg   936
Asp Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Ser Thr Ala Val
            260                 265                 270

cag gtc cac gat gtc tgc gtc tgc cag cac aac act gcc ggc cca aat   984
Gln Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn
        275                 280                 285

tgt gag cgc tgt gca ccc ttc tac aac aac cgg ccc tgg aga ccg gcg   1032
Cys Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala
    290                 295                 300

gag ggc cag gac gcc cat gaa tgc caa agg tgc gac tgc aat ggg cac   1080
```

```
Glu Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His
305                 310                 315                 320

tca gag aca tgt cac ttt gac ccc gct gtg ttt gcc gcc agc cag ggg   1128
Ser Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly
                325                 330                 335

gca tat gga ggt gtg tgt gac aat tgc cgg gac cac acc gaa ggc aag   1176
Ala Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys
            340                 345                 350

aac tgt gag cgg tgt cag ctg cac tat ttc cgg aac cgg cgc ccg gga   1224
Asn Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly
        355                 360                 365

gct tcc att cag gag acc tgc atc tcc tgc gag tgt gat ccg gat ggg   1272
Ala Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly
    370                 375                 380

gca gtc gca ggg gct ccc tgt gac cca gtg acc ggg cag tgt gtg tgc   1320
Ala Val Ala Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys
385                 390                 395                 400

aag gag cat gtg cag gga gag cgc tgt gac cta tgc aag ccg ggc ttc   1368
Lys Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe
                405                 410                 415

act gga ctc acc tac gcc aac ccg cga cgg tgc cac cgc tgt gac tgc   1416
Thr Gly Leu Thr Tyr Ala Asn Pro Arg Arg Cys His Arg Cys Asp Cys
            420                 425                 430

aac atc ctg ggg tcc cgg gag atg ccg tgt gac gag gag agt ggg cgc   1464
Asn Ile Leu Gly Ser Arg Glu Met Pro Cys Asp Glu Glu Ser Gly Arg
        435                 440                 445

tgc ctt tgt ctg ccc aac gtg gtg ggt ccc aaa tgt gac cag tgt gct   1512
Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala
    450                 455                 460

ccc tac cac tgg aag ctg gcc agt ggc cag ggc tgt gaa ccg tgt gcc   1560
Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala
465                 470                 475                 480

tgc gac ccg cac aac tcc ctc agc cca cag tgc aac cag ttc aca ggg   1608
Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly
                485                 490                 495

cag tgc ccc tgt cgg gaa ggc ttt ggt ggc ctg atg tgc agc gct gca   1656
Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala
            500                 505                 510

gcc atc cgc cag tgt cca gac cgg acc tat gga gac gtg gcc aca gga   1704
Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly
        515                 520                 525

tgc cga gcc tgt gac tgt gat ttc cgg gga aca gag ggc ccg ggc tgc   1752
Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys
    530                 535                 540

gac aag gca tca ggc cgc tgc ctc tgc cgc cct ggc ttg acc ggg ccc   1800
Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro
```

```
545                 550                 555                 560

cgc tgt gac cag tgc cag cga ggc tac tgc aat cgc tac ccg gtg tgc   1848
Arg Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val Cys
                565                 570                 575

gtg gcc tgc cac cct tgc ttc cag acc tat gat gcg gac ctc cgg gag   1896
Val Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg Glu
            580                 585                 590

cag gcc ctg cgc ttt ggt aga ctc ccg aat gcc acc gcc agc ctg tgg   1944
Gln Ala Leu Arg Phe Gly Arg Leu Pro Asn Ala Thr Ala Ser Leu Trp
        595                 600                 605

tca ggg cct ggg ctg gag gac cgt ggc ctg gcc tcc cgg atc cta gat   1992
Ser Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu Asp
    610                 615                 620

gca aag agt aag att gag cag atc cga gca gtt ctc agc agc ccc gca   2040
Ala Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro Ala
625                 630                 635                 640

gtc aca gag cag gag gtg gct cag gtg gcc agt gcc atc ctc tcc ctc   2088
Val Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser Leu
                645                 650                 655

agg cga act ctc cag ggc ctg cag ctg gat ctg ccc ctg gag gag gag   2136
Arg Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu Glu
            660                 665                 670

acg ttg tcc ctt ccg aga gac ctg gag agt ctt gac aga agc ttc aat   2184
Thr Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe Asn
        675                 680                 685

ggt ctc ctt act atg tat cag agg aag agg gag cag ttt gaa aaa ata   2232
Gly Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys Ile
    690                 695                 700

agc agt gct gat cct tca gga gcc ttc cgg atg ctg agc aca gcc tac   2280
Ser Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala Tyr
705                 710                 715                 720

gag cag tca gcc cag gct gct cag cag gtc tcc gac agc tcg cgc ctt   2328
Glu Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg Leu
                725                 730                 735

ttg gac cag ctc agg gac agc cgg aga gag gca gag agg ctg gtg cgg   2376
Leu Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val Arg
            740                 745                 750

cag gcg gga gga gga gga ggc acc ggc agc ccc aag ctt gtg gcc ctg   2424
Gln Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala Leu
        755                 760                 765

agg ttg gag atg tct tcg ttg cct gac ctg aca ccc acc ttc aac aag   2472
Arg Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn Lys
    770                 775                 780

ctc tgt ggc aac tcc agg cag atg gct tgc acc cca ata tca tgc cct   2520
Leu Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys Pro
785                 790                 795                 800
```

```
ggt gag cta tgt ccc caa gac aat ggc aca gcc tgt gcg tcc cgc tgc   2568
Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Ala Ser Arg Cys
                805                 810                 815

agg ggt gtc ctt ccc agg gcc ggt ggg gcc ttc ttg atg gcg ggg cag   2616
Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln
            820                 825                 830

gtg gct gag cag ctg cgg ggc ttc aat gcc cag ctc cag cgg acc agg   2664
Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg
        835                 840                 845

cag atg att agg gca gcc gag gaa tct gcc tca cag att caa tcc agt   2712
Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser
    850                 855                 860

gcc cag cgc ttg gag acc cag gtg agc gcc agc cgc tcc cag atg gag   2760
Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu
865                 870                 875                 880

gaa gat gtc aga cgc aca cgg ctc cta atc cag cag gtc cgg gac ttc   2808
Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe
                885                 890                 895

cta aca gac ccc gac act gat gca gcc act atc cag gag gtc agc gag   2856
Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu
            900                 905                 910

gcc gtg ctg gcc ctg tgg ctg ccc aca gac tca gct act gtt ctg cag   2904
Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln
        915                 920                 925

aag atg aat gag atc cag gcc att gca gcc agg ctc ccc aac gtg gac   2952
Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp
    930                 935                 940

ttg gtg ctg tcc cag acc aag cag gac att gcg cgt gcc cgc cgg ttg   3000
Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu
945                 950                 955                 960

cag gct gag gct gag gaa gcc agg agc cga gcc cat gca gtg gag ggc   3048
Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly
                965                 970                 975

cag gtg gag gat gtg gtt ggg aac ctg cgg cag ggg aca gtg gca ctg   3096
Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu
            980                 985                 990

cag gaa gct cag gac acc atg caa ggc acc agc cgg tcc ctt cgg ctt   3144
Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu
        995                1000                1005

atc cag gac agg gtt gct gag gtt cag cag gta ctg cgg cca gca gaa   3192
Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu
   1010                1015                1020

aag ctg gtg aca agc atg acc aag cag ctg ggt gac ttc tgg aca cgg   3240
Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg
1025                1030                1035                1040
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atg gag gag ctc cgc cac caa gcc cgg cag cag ggg gca gag gca gtc   3288
Met Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val
                1045                1050                1055

cag gcc cag cag ctt gcg gaa ggt gcc agc gag cag gca ttg agt gcc   3336
Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala
            1060                1065                1070

caa gag gga ttt gag aga ata aaa caa aag tat gct gag ttg aag gac   3384
Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp
        1075                1080                1085

cgg ttg ggt cag agt tcc atg ctg ggt gag cag ggt gcc cgg atc cag   3432
Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln
    1090                1095                1100

agt gtg aag aca gag gca gag gag ctg ttt ggg gag acc atg gag atg   3480
Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met
1105                1110                1115                1120

atg gac agg atg aaa gac atg gag ttg gag ctg ctg cgg ggc agc cag   3528
Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser Gln
                1125                1130                1135

gcc atc atg ctg cgc tca gcg gac ctg aca gga ctg gag aag cgt gtg   3576
Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg Val
            1140                1145                1150

gag cag atc cgt gac cac atc aat ggg cgc gtg ctc tac tat gcc acc   3624
Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala Thr
        1155                1160                1165

tgc aag tgatgctaca cgttccagcc cgttgcccca ctcatctgcg cgctttgctt    3680
Cys Lys
    1170

ttggttgggg ggcagattgg gttggaatgc tttccatctc caggagactt tcatgtagcc 3740

caaagtacag cctggaccac ccctggtgtg tgtagctagt aagattaccc tgagctgcag 3800

ctgagcctga gccaatggga cagttacact tgacagacaa agatggtgga gattggcatg 3860

ccattgaaac taagagctct caagtcaagg aagctgggct gggcagtatc ccccgccttt 3920

agttctccac                                                        3930
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Met Arg Pro Phe Phe Leu Leu Cys Phe Ala Leu Pro Gly Leu Leu His
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Ala Gln Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp
            20                  25                  30

Leu Leu Val Gly Arg Thr Arg Phe L u Arg Ala Ser Ser Thr Cys Gly
        35                  40                  45
```

```
Leu Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met
     50                  55                  60

Lys Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His
 65                  70                  75                  80

Arg Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln
                 85                  90                  95

Ser Gln Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg
            100                 105                 110

Arg Phe Gln Leu Gln Glu Val Met Met Glu Phe Arg Gly Pro Met Pro
        115                 120                 125

Ala Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg
    130                 135                 140

Val Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val
145                 150                 155                 160

Arg Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu
                165                 170                 175

Pro Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn
            180                 185                 190

Leu Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile
        195                 200                 205

Gln Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu
    210                 215                 220

Ala Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala
225                 230                 235                 240

Val Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala
                245                 250                 255

Asp Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Ser Thr Ala Val
            260                 265                 270

Gln Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn
        275                 280                 285

Cys Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala
    290                 295                 300

Glu Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His
305                 310                 315                 320

Ser Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly
                325                 330                 335

Ala Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys
            340                 345                 350

Asn Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly
        355                 360                 365
```

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Ala Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly
    370                 375                 380

Ala Val Ala Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys
385                 390                 395                 400

Lys Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe
                405                 410                 415

Thr Gly Leu Thr Tyr Ala Asn Pro Arg Arg Cys His Arg Cys Asp Cys
            420                 425                 430

Asn Ile Leu Gly Ser Arg Glu Met Pro Cys Asp Glu Glu Ser Gly Arg
        435                 440                 445

Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala
    450                 455                 460

Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala
465                 470                 475                 480

Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly
                485                 490                 495

Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala
            500                 505                 510

Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly
        515                 520                 525

Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys
    530                 535                 540

Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro
545                 550                 555                 560

Arg Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val Cys
                565                 570                 575

Val Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg Glu
            580                 585                 590

Gln Ala Leu Arg Phe Gly Arg Leu Pro Asn Ala Thr Ala Ser Leu Trp
        595                 600                 605

Ser Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu Asp
    610                 615                 620

Ala Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro Ala
625                 630                 635                 640

Val Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser Leu
                645                 650                 655

Arg Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu Glu
            660                 665                 670

Thr Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe Asn
        675                 680                 685

Gly Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys Ile
```

690 695 700

Ser Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala Tyr
705 710 715 720

Glu Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg Leu
725 730 735

Leu Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val Arg
740 745 750

Gln Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala Leu
755 760 765

Arg Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn Lys
770 775 780

Leu Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys Pro
785 790 795 800

Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Ala Ser Arg Cys
805 810 815

Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln
820 825 830

Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg
835 840 845

Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser
850 855 860

Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu
865 870 875 880

Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe
885 890 895

Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu
900 905 910

Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln
915 920 925

Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp
930 935 940

Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu
945 950 955 960

Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly
965 970 975

Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu
980 985 990

Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu
995 1000 1005

Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu
1010 1015 1020

```
Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg
1025                1030                1035                1040

Met Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val
                1045                1050                1055

Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala
            1060                1065                1070

Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp
        1075                1080                1085

Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln
    1090                1095                1100

Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met
1105                1110                1115                1120

Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser Gln
                1125                1130                1135

Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg Val
            1140                1145                1150

Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala Thr
        1155                1160                1165

Cys Lys
    1170


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<222> (1)..(3459)

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caa caa gcc tgc tcc cgt ggg gcc tgc tat cca cct gtt ggg gac ctg   48
Gln Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp Leu
  1               5                  10                  15

ctt gtt ggg agg acc cgg ttt ctc cga gct tca tct acc tgt gga ctg   96
Leu Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly Leu
             20                  25                  30

acc aag cct gag acc tac tgc acc cag tat ggc gag tgg cag atg aaa   144
Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met Lys
         35                  40                  45

tgc tgc aag tgt gac tcc agg cag cct cac aac tac tac agt cac cga   192
Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His Arg
     50                  55                  60

gta gag aat gtg gct tca tcc tcc ggc ccc atg cgc tgg tgg cag tcc   240
Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln Ser
 65                  70                  75                  80
```

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cag aat gat gtg aac cct gtc tct ctg cag ctg gac ctg gac agg aga   288
Gln Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg Arg
                85                  90                  95

ttc cag ctt caa gaa gtc atg atg gag ttc cga ggg ccc atg cct gcc   336
Phe Gln Leu Gln Glu Val Met Met Glu Phe Arg Gly Pro Met Pro Ala
            100                 105                 110

ggc atg ctg att gag cgc tcc tca gac ttc ggt aag acc tgg cga gtg   384
Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg Val
        115                 120                 125

tac cag tac ctg gct gcc gac tgc acc tcc acc ttc cct cgg gtc cgc   432
Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val Arg
    130                 135                 140

cag ggt cgg cct cag agc tgg cag gat gtt cgg tgc cag tcc ctg cct   480
Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu Pro
145                 150                 155                 160

cag agg cct aat gca cgc cta aat ggg ggg aag gtc caa ctt aac ctt   528
Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn Leu
                165                 170                 175

atg gat tta gtg tct ggg att cca gca act caa agt caa aaa att caa   576
Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln
            180                 185                 190

gag gtg ggg gag atc aca aac ttg aga gtc aat ttc acc agg ctg gcc   624
Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu Ala
        195                 200                 205

cct gtg ccc caa agg ggc tac cac cct ccc agc gcc tac tat gct gtg   672
Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val
    210                 215                 220

tcc cag ctc cgt ctg cag ggg agc tgc ttc tgt cac ggc cat gct gat   720
Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala Asp
225                 230                 235                 240

cgc tgc gca ccc aag cct ggg gcc tct gca ggc tcc acc gct gtg cag   768
Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Ser Thr Ala Val Gln
                245                 250                 255

gtc cac gat gtc tgc gtc tgc cag cac aac act gcc ggc cca aat tgt   816
Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn Cys
            260                 265                 270

gag cgc tgt gca ccc ttc tac aac aac cgg ccc tgg aga ccg gcg gag   864
Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala Glu
        275                 280                 285

ggc cag gac gcc cat gaa tgc caa agg tgc gac tgc aat ggg cac tca   912
Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His Ser
    290                 295                 300

gag aca tgt cac ttt gac ccc gct gtg ttt gcc gcc agc cag ggg gca   960
Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly Ala
305                 310                 315                 320
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tat gga ggt gtg tgt gac aat tgc cgg gac cac acc gaa ggc aag aac   1008
Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys Asn
                325                 330                 335

tgt gag cgg tgt cag ctg cac tat ttc cgg aac cgg cgc ccg gga gct   1056
Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly Ala
            340                 345                 350

tcc att cag gag acc tgc atc tcc tgc gag tgt gat ccg gat ggg gca   1104
Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly Ala
        355                 360                 365

gtc gca ggg gct ccc tgt gac cca gtg acc ggg cag tgt gtg tgc aag   1152
Val Ala Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys Lys
    370                 375                 380

gag cat gtg cag gga gag cgc tgt gac cta tgc aag ccg ggc ttc act   1200
Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe Thr
385                 390                 395                 400

gga ctc acc tac gcc aac ccg cga cgg tgc cac cgc tgt gac tgc aac   1248
Gly Leu Thr Tyr Ala Asn Pro Arg Arg Cys His Arg Cys Asp Cys Asn
                405                 410                 415

atc ctg ggg tcc cgg gag atg ccg tgt gac gag gag agt ggg cgc tgc   1296
Ile Leu Gly Ser Arg Glu Met Pro Cys Asp Glu Glu Ser Gly Arg Cys
            420                 425                 430

ctt tgt ctg ccc aac gtg gtg ggt ccc aaa tgt gac cag tgt gct ccc   1344
Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala Pro
        435                 440                 445

tac cac tgg aag ctg gcc agt ggc cag ggc tgt gaa ccg tgt gcc tgc   1392
Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala Cys
    450                 455                 460

gac ccg cac aac tcc ctc agc cca cag tgc aac cag ttc aca ggg cag   1440
Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly Gln
465                 470                 475                 480

tgc ccc tgt cgg gaa ggc ttt ggt ggc ctg atg tgc agc gct gca gcc   1488
Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala Ala
                485                 490                 495

atc cgc cag tgt cca gac cgg acc tat gga gac gtg gcc aca gga tgc   1536
Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly Cys
            500                 505                 510

cga gcc tgt gac tgt gat ttc cgg gga aca gag ggc ccg ggc tgc gac   1584
Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys Asp
        515                 520                 525

aag gca tca ggc cgc tgc ctc tgc cgc cct ggc ttg acc ggg ccc cgc   1632
Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro Arg
    530                 535                 540

tgt gac cag tgc cag cga ggc tac tgc aat cgc tac ccg gtg tgc gtg   1680
Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val Cys Val
545                 550                 555                 560

gcc tgc cac cct tgc ttc cag acc tat gat gcg gac ctc cgg gag cag   1728
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Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg Glu Gln
                565                 570                 575

gcc ctg cgc ttt ggt aga ctc ccg aat gcc acc gcc agc ctg tgg tca   1776
Ala Leu Arg Phe Gly Arg Leu Pro Asn Ala Thr Ala Ser Leu Trp Ser
            580                 585                 590

ggg cct ggg ctg gag gac cgt ggc ctg gcc tcc cgg atc cta gat gca   1824
Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu Asp Ala
        595                 600                 605

aag agt aag att gag cag atc cga gca gtt ctc agc agc ccc gca gtc   1872
Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro Ala Val
    610                 615                 620

aca gag cag gag gtg gct cag gtg gcc agt gcc atc ctc tcc ctc agg   1920
Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser Leu Arg
625                 630                 635                 640

cga act ctc cag ggc ctg cag ctg gat ctg ccc ctg gag gag gag acg   1968
Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu Glu Thr
                645                 650                 655

ttg tcc ctt ccg aga gac ctg gag agt ctt gac aga agc ttc aat ggt   2016
Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe Asn Gly
            660                 665                 670

ctc ctt act atg tat cag agg aag agg gag cag ttt gaa aaa ata agc   2064
Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys Ile Ser
        675                 680                 685

agt gct gat cct tca gga gcc ttc cgg atg ctg agc aca gcc tac gag   2112
Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala Tyr Glu
    690                 695                 700

cag tca gcc cag gct gct cag cag gtc tcc gac agc tcg cgc ctt ttg   2160
Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg Leu Leu
705                 710                 715                 720

gac cag ctc agg gac agc cgg aga gag gca gag agg ctg gtg cgg cag   2208
Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val Arg Gln
                725                 730                 735

gcg gga gga gga gga ggc acc ggc agc ccc aag ctt gtg gcc ctg agg   2256
Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala Leu Arg
            740                 745                 750

ttg gag atg tct tcg ttg cct gac ctg aca ccc acc ttc aac aag ctc   2304
Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn Lys Leu
        755                 760                 765

tgt ggc aac tcc agg cag atg gct tgc acc cca ata tca tgc cct ggt   2352
Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys Pro Gly
    770                 775                 780

gag cta tgt ccc caa gac aat ggc aca gcc tgt gcg tcc cgc tgc agg   2400
Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Ala Ser Arg Cys Arg
785                 790                 795                 800

ggt gtc ctt ccc agg gcc ggt ggg gcc ttc ttg atg gcg ggg cag gtg   2448
Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln Val
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                805                 810                 815

gct gag cag ctg cgg ggc ttc aat gcc cag ctc cag cgg acc agg cag   2496
Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg Gln
            820                 825                 830

atg att agg gca gcc gag gaa tct gcc tca cag att caa tcc agc gcc   2544
Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser Ala
        835                 840                 845

cag cgc ttg gag acc cag gtg agc gcc agc cgc tcc cag atg gag gaa   2592
Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu Glu
    850                 855                 860

gat gtc aga cgc aca cgg ctc cta atc cag cag gtc cgg gac ttc cta   2640
Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe Leu
865                 870                 875                 880

aca gac ccc gac act gat gca gcc act atc cag gag gtc agc gag gcc   2688
Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu Ala
                885                 890                 895

gtg ctg gcc ctg tgg ctg ccc aca gac tca gct act gtt ctg cag aag   2736
Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln Lys
            900                 905                 910

atg aat gag atc cag gcc att gca gcc agg ctc ccc aac gtg gac ttg   2784
Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp Leu
        915                 920                 925

gtg ctg tcc cag acc aag cag gac att gcg cgt gcc cgc cgg ttg cag   2832
Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu Gln
    930                 935                 940

gct gag gct gag gaa gcc agg agc cga gcc cat gca gtg gag ggc cag   2880
Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly Gln
945                 950                 955                 960

gtg gag gat gtg gtt ggg aac ctg cgg cag ggg aca gtg gca ctg cag   2928
Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu Gln
                965                 970                 975

gaa gct cag gac acc atg caa ggc acc agc cgg tcc ctt cgg ctt atc   2976
Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu Ile
            980                 985                 990

cag gac agg gtt gct gag gtt cag cag gta ctg cgg cca gca gaa aag   3024
Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu Lys
        995                1000                1005

ctg gtg aca agc atg acc aag cag ctg ggt gac ttc tgg aca cgg atg   3072
Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg Met
   1010                1015                1020

gag gag ctc cgc cac caa gcc cgg cag cag ggg gca gag gca gtc cag   3120
Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val Gln
1025                1030                1035                1040

gcc cag cag ctt gcg gaa ggt gcc agc gag cag gca ttg agt gcc caa   3168
Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala Gln
                1045                1050                1055
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gag gga ttt gag aga ata aaa caa aag tat gct gag ttg aag gac cgg   3216
Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp Arg
          1060                1065                1070

ttg ggt cag agt tcc atg ctg ggt gag cag ggt gcc cgg atc cag agt   3264
Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln Ser
       1075                1080                1085

gtg aag aca gag gca gag gag ctg ttt ggg gag acc atg gag atg atg   3312
Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met Met
   1090                1095                1100

gac agg atg aaa gac atg gag ttg gag ctg ctg cgg ggc agc cag gcc   3360
Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser Gln Ala
1105                1110                1115                1120

atc atg ctg cgc tca gcg gac ctg aca gga ctg gag aag cgt gtg gag   3408
Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg Val Glu
               1125                1130                1135

cag atc cgt gac cac atc aat ggg cgc gtg ctc tac tat gcc acc tgc   3456
Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala Thr Cys
          1140                1145                1150

aag tgatgctaca cgttccagcc cgttgcccca ctcatctgcg cgctttgctt        3509
Lys

ttggttgggg ggcagattgg gttggaatgc tttccatctc caggagactt tcatgtagcc 3569

caaagtacag cctggaccac ccctggtgtg tgtagctagt aagattaccc tgagctgcag 3629

ctgagcctga gccaatggga cagttacact tgacagacaa agatggtgga gattggcatg 3689

ccattgaaac taagagctct caagtcaagg aagctgggct gggcagtatc ccccgccttt 3749

agttctccac                                                        3759
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Leu Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly Leu
             20                  25                  30

Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met Lys
         35                  40                  45

Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His Arg
     50                  55                  60

Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln Ser
 65                  70                  75                  80

Gln Asn Asp Val Asn Pro Val S r Leu Gln Leu Asp Leu Asp Arg Arg
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85 90 95

Phe Gln Leu Gln Glu Val Met Met Glu Phe Arg Gly Pro Met Pro Ala
100 105 110

Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg Val
115 120 125

Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val Arg
130 135 140

Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu Pro
145 150 155 160

Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn Leu
165 170 175

Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln
180 185 190

Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu Ala
195 200 205

Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val
210 215 220

Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala Asp
225 230 235 240

Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Ser Thr Ala Val Gln
245 250 255

Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn Cys
260 265 270

Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala Glu
275 280 285

Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His Ser
290 295 300

Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly Ala
305 310 315 320

Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys Asn
325 330 335

Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly Ala
340 345 350

Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly Ala
355 360 365

Val Ala Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys Lys
370 375 380

Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe Thr
385 390 395 400

Gly L u Thr Tyr Ala Asn Pro Arg Arg Cys His Arg Cys Asp Cys Asn
405 410 415

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Ile Leu Gly Ser Arg Glu Met Pro Cys Asp Glu Glu Ser Gly Arg Cys
            420                 425                 430

Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala Pro
        435                 440                 445

Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala Cys
    450                 455                 460

Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly Gln
465                 470                 475                 480

Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala Ala
                485                 490                 495

Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly Cys
            500                 505                 510

Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys Asp
        515                 520                 525

Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro Arg
    530                 535                 540

Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val Cys Val
545                 550                 555                 560

Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg Glu Gln
                565                 570                 575

Ala Leu Arg Phe Gly Arg Leu Pro Asn Ala Thr Ala Ser Leu Trp Ser
            580                 585                 590

Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu Asp Ala
        595                 600                 605

Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro Ala Val
    610                 615                 620

Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser Leu Arg
625                 630                 635                 640

Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu Glu Thr
                645                 650                 655

Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe Asn Gly
            660                 665                 670

Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys Ile Ser
        675                 680                 685

Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala Tyr Glu
    690                 695                 700

Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg Leu Leu
705                 710                 715                 720

Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val Arg Gln
                725                 730                 735
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Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala Leu Arg
            740                 745                 750

Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn Lys Leu
        755                 760                 765

Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys Pro Gly
    770                 775                 780

Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Ala Ser Arg Cys Arg
785                 790                 795                 800

Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln Val
                805                 810                 815

Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg Gln
            820                 825                 830

Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser Ala
        835                 840                 845

Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu Glu
    850                 855                 860

Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe Leu
865                 870                 875                 880

Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu Ala
                885                 890                 895

Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln Lys
            900                 905                 910

Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp Leu
        915                 920                 925

Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu Gln
    930                 935                 940

Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly Gln
945                 950                 955                 960

Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu Gln
                965                 970                 975

Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu Ile
            980                 985                 990

Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu Lys
        995                1000                1005

Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg Met
   1010                1015                1020

Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val Gln
1025                1030                1035                1040

Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala Gln
                1045                1050                1055

Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp Arg
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          1060                1065                1070

Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln Ser
       1075                1080                1085

Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met Met
   1090                1095                1100

Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser Gln Ala
1105                1110                1115                1120

Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg Val Glu
               1125                1130                1135

Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala Thr Cys
           1140                1145                1150

Lys
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<400> 17

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atg agg gcc tgg atc ttc ttt ctc ctt tgc ctg gcc ggg agg gct ctg  107
Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu
  1               5                  10                  15

gca gcc cca cta gcc gac tac aag gac gac gat gac aag cta gcc caa  155
Ala Ala Pro Leu Ala Asp Tyr Lys Asp Asp Asp Asp Lys Leu Ala Gln
             20                  25                  30

caa gcc tgc tcc cgt ggg gcc tgc tat cca cct gtt ggg gac ctg ctt  203
Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp Leu Leu
         35                  40                  45

gtt ggg agg acc cgg ttt ctc cga gct tca tct acc tgt gga ctg acc  251
Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly Leu Thr
     50                  55                  60

aag cct gag acc tac tgc acc cag tat ggc gag tgg cag atg aaa tgc  299
Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met Lys Cys
 65                  70                  75                  80
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tgc aag tgt gac tcc agg cag cct cac aac tac tac agt cac cga gta   347
Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His Arg Val
                 85                  90                  95

gag aat gtg gct tca tcc tcc ggc ccc atg cgc tgg tgg cag tcc cag   395
Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln Ser Gln
            100                 105                 110

aat gat gtg aac cct gtc tct ctg cag ctg gac ctg gac agg aga ttc   443
Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg Arg Phe
        115                 120                 125

cag ctt caa gaa gtc atg atg gag ttc cag ggg ccc atg cct gcc ggc   491
Gln Leu Gln Glu Val Met Met Glu Phe Gln Gly Pro Met Pro Ala Gly
    130                 135                 140

atg ctg att gag cgc tcc tca gac ttc ggt aag acc tgg cga gtg tac   539
Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg Val Tyr
145                 150                 155                 160

cag tac ctg gct gcc gac tgc acc tcc acc ttc cct cgg gtc cgc cag   587
Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val Arg Gln
                165                 170                 175

ggt cgg cct cag agc tgg cag gat gtt cgg tgc cag tcc ctg cct cag   635
Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu Pro Gln
            180                 185                 190

agg cct aat gca cgc cta aat ggg ggg aag gtc caa ctt aac ctt atg   683
Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn Leu Met
        195                 200                 205

gat tta gtg tct ggg att cca gca act caa agt caa aaa att caa gag   731
Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln Glu
    210                 215                 220

gtg ggg gag atc aca aac ttg aga gtc aat ttc acc agg ctg gcc cct   779
Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu Ala Pro
225                 230                 235                 240

gtg ccc caa agg ggc tac cac cct ccc agc gcc tac tat gct gtg tcc   827
Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val Ser
                245                 250                 255

cag ctc cgt ctg cag ggg agc tgc ttc tgt cac ggc cat gct gat cgc   875
Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala Asp Arg
            260                 265                 270

tgc gca ccc aag cct ggg gcc tct gca ggc ccc tcc acc gct gtg cag   923
Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Pro Ser Thr Ala Val Gln
        275                 280                 285

gtc cac gat gtc tgc gtc tgc cag cac aac act gcc ggc cca aat tgt   971
Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn Cys
    290                 295                 300

gag cgc tgt gca ccc ttc tac aac aac cgg ccc tgg aga ccg gcg gag   1019
Glu Arg Cys Ala Pro Ph  Tyr Asn Asn Arg Pro Trp Arg Pro Ala Glu
305                 310                 315                 320

ggc cag gac gcc cat gaa tgc caa agg tgc gac tgc aat ggg cac tca   1067
```

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Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His Ser
                325                 330                 335

gag aca tgt cac ttt gac ccc gct gtg ttt gcc gcc agc cag ggg gca   1115
Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly Ala
            340                 345                 350

tat gga ggt gtg tgt gac aat tgc cgg gac cac acc gaa ggc aag aac   1163
Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys Asn
        355                 360                 365

tgt gag cgg tgt cag ctg cac tat ttc cgg aac cgg cgc ccg gga gct   1211
Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly Ala
    370                 375                 380

tcc att cag gag acc tgc atc tcc tgc gag tgt gat ccg gat ggg gca   1259
Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly Ala
385                 390                 395                 400

gtg cca ggg gct ccc tgt gac cca gtg acc ggg cag tgt gtg tgc aag   1307
Val Pro Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys Lys
                405                 410                 415

gag cat gtg cag gga gag cgc tgt gac cta tgc aag ccg ggc ttc act   1355
Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe Thr
            420                 425                 430

gga ctc acc tac gcc aac ccg cag ggc tgc cac cgc tgt gac tgc aac   1403
Gly Leu Thr Tyr Ala Asn Pro Gln Gly Cys His Arg Cys Asp Cys Asn
        435                 440                 445

atc ctg ggg tcc cgg agg gac atg ccg tgt gac gag gag agt ggg cgc   1451
Ile Leu Gly Ser Arg Arg Asp Met Pro Cys Asp Glu Glu Ser Gly Arg
    450                 455                 460

tgc ctt tgt ctg ccc aac gtg gtg ggt ccc aaa tgt gac cag tgt gct   1499
Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala
465                 470                 475                 480

ccc tac cac tgg aag ctg gcc agt ggc cag ggc tgt gaa ccg tgt gcc   1547
Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala
                485                 490                 495

tgc gac ccg cac aac tcc ctc agc cca cag tgc aac cag ttc aca ggg   1595
Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly
            500                 505                 510

cag tgc ccc tgt cgg gaa ggc ttt ggt ggc ctg atg tgc agc gct gca   1643
Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala
        515                 520                 525

gcc atc cgc cag tgt cca gac cgg acc tat gga gac gtg gcc aca gga   1691
Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly
    530                 535                 540

tgc cga gcc tgt gac tgt gat ttc cgg gga aca gag ggc ccg ggc tgc   1739
Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys
545                 550                 555                 560

gac aag gca tca ggc cgc tgc ctc tgc cgc cct ggc ttg acc ggg ccc   1787
Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro
```

```
ggt gag cta tgt ccc caa gac aat ggc aca gcc tgt ggc tcc cgc tgc   2555
Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Gly Ser Arg Cys
            820                 825                 830

agg ggt gtc ctt ccc agg gcc ggt ggg gcc ttc ttg atg gcg ggg cag   2603
Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln
        835                 840                 845

gtg gct gag cag ctg cgg ggc ttc aat gcc cag ctc cag cgg acc agg   2651
Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg
    850                 855                 860

cag atg att agg gca gcc gag gaa tct gcc tca cag att caa tcc agt   2699
Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser
865                 870                 875                 880

gcc cag cgc ttg gag acc cag gtg agc gcc agc cgc tcc cag atg gag   2747
Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu
                885                 890                 895

gaa gat gtc aga cgc aca cgg ctc cta atc cag cag gtc cgg gac ttc   2795
Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe
            900                 905                 910

cta aca gac ccc gac act gat gca gcc act atc cag gag gtc agc gag   2843
Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu
        915                 920                 925

gcc gtg ctg gcc ctg tgg ctg ccc aca gac tca gct act gtt ctg cag   2891
Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln
    930                 935                 940

aag atg aat gag atc cag gcc att gca gcc agg ctc ccc aac gtg gac   2939
Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp
945                 950                 955                 960

ttg gtg ctg tcc cag acc aag cag gac att gcg cgt gcc cgc cgg ttg   2987
Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu
                965                 970                 975

cag gct gag gct gag gaa gcc agg agc cga gcc cat gca gtg gag ggc   3035
Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly
            980                 985                 990

cag gtg gaa gat gtg gtt ggg aac ctg cgg cag ggg aca gtg gca ctg   3083
Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu
        995                1000                1005

cag gaa gct cag gac acc atg caa ggc acc agc cgc tcc ctt cgg ctt   3131
Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu
   1010                1015                1020

atc cag gac agg gtt gct gag gtt cag cag gta ctg cgg cca gca gaa   3179
Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu
1025                1030                1035                1040

aag ctg gtg aca agc atg acc aag cag ctg ggt gac ttc tgg aca cgg   3227
Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg
                1045                1050                1055
```

```
atg gag gag ctc cgc cac caa gcc cgg cag cag ggg gca gag gca gtc   3275
Met Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val
          1060                1065                1070

cag gcc cag cag ctt gcg gaa ggt gcc agc gag cag gca ttg agt gcc   3323
Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala
       1075                1080                1085

caa gag gga ttt gag aga ata aaa caa aag tat gct gag ttg aag gac   3371
Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp
   1090                1095                1100

cgg ttg ggt cag agt tcc atg ctg ggt gag cag ggt gcc cgg atc cag   3419
Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln
1105                1110                1115                1120

agt gtg aag aca gag gca gag gag ctg ttt ggg gag acc atg gag atg   3467
Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met
               1125                1130                1135

atg gac agg atg aaa gac atg gag ttg gag ctg ctg cgg ggc agc cag   3515
Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser Gln
          1140                1145                1150

gcc atc atg ctg cgc tca gcg gac ctg aca gga ctg gag aag cgt gtg   3563
Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg Val
       1155                1160                1165

gag cag atc cgt gac cac atc aat ggg cgc gtg ctc tac tat gcc acc   3611
Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala Thr
   1170                1175                1180

tgc aag tgat                                                     3621
Cys Lys
1185
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<213> Homo sapiens

<400> 18

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Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu
  1               5                  10                  15

Ala Ala Pro Leu Ala Asp Tyr Lys Asp Asp Asp Asp Lys Leu Ala Gln
             20                  25                  30

Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp Leu Leu
         35                  40                  45

Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly Leu Thr
     50                  55                  60

Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met Lys Cys
 65                  70                  75                  80

Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His Arg Val
                 85                  90                  95
```

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Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln Ser Gln
            100                 105                 110

Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg Arg Phe
        115                 120                 125

Gln Leu Gln Glu Val Met Met Glu Phe Gln Gly Pro Met Pro Ala Gly
    130                 135                 140

Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg Val Tyr
145                 150                 155                 160

Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val Arg Gln
                165                 170                 175

Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu Pro Gln
            180                 185                 190

Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn Leu Met
        195                 200                 205

Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln Glu
    210                 215                 220

Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu Ala Pro
225                 230                 235                 240

Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val Ser
                245                 250                 255

Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala Asp Arg
            260                 265                 270

Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Pro Ser Thr Ala Val Gln
        275                 280                 285

Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn Cys
    290                 295                 300

Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala Glu
305                 310                 315                 320

Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His Ser
                325                 330                 335

Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly Ala
            340                 345                 350

Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys Asn
        355                 360                 365

Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly Ala
    370                 375                 380

Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly Ala
385                 390                 395                 400

Val Pro Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys Lys
                405                 410                 415

Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe Thr
```

```
            420                 425                 430

Gly Leu Thr Tyr Ala Asn Pro Gln Gly Cys His Arg Cys Asp Cys Asn
        435                 440                 445

Ile Leu Gly Ser Arg Arg Asp Met Pro Cys Asp Glu Glu Ser Gly Arg
    450                 455                 460

Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala
465                 470                 475                 480

Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala
                485                 490                 495

Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly
            500                 505                 510

Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala
        515                 520                 525

Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly
    530                 535                 540

Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys
545                 550                 555                 560

Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro
                565                 570                 575

Arg Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val Cys
            580                 585                 590

Val Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg Glu
        595                 600                 605

Gln Ala Leu Arg Phe Gly Arg Leu Arg Asn Ala Thr Ala Ser Leu Trp
    610                 615                 620

Ser Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu Asp
625                 630                 635                 640

Ala Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro Ala
                645                 650                 655

Val Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser Leu
            660                 665                 670

Arg Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu Glu
        675                 680                 685

Thr Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe Asn
    690                 695                 700

Gly Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys Ile
705                 710                 715                 720

Ser Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala Tyr
                725                 730                 735

Glu Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg Leu
            740                 745                 750
```

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Leu Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val Arg
        755                 760                 765

Gln Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala Leu
    770                 775                 780

Arg Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn Lys
785                 790                 795                 800

Leu Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys Pro
                805                 810                 815

Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Gly Ser Arg Cys
            820                 825                 830

Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln
        835                 840                 845

Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg
    850                 855                 860

Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser
865                 870                 875                 880

Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu
                885                 890                 895

Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe
            900                 905                 910

Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu
        915                 920                 925

Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln
    930                 935                 940

Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp
945                 950                 955                 960

Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu
                965                 970                 975

Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly
            980                 985                 990

Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu
        995                1000                1005

Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu
   1010                1015                1020

Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu
1025                1030                1035                1040

Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg
                1045                1050                1055

M t Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val
            1060                1065                1070
```

```
Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala
       1075                1080                1085

Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp
   1090                1095                1100

Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln
1105                1110                1115                1120

Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met
               1125                1130                1135

Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser Gln
           1140                1145                1150

Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg Val
       1155                1160                1165

Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala Thr
   1170                1175                1180

Cys Lys
1185


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<222> (13)..(36)

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gcccca cta gcc gac tac aag gac gac gat gac aag cta gcc caa caa    48
       Leu Ala Asp Tyr Lys Asp Asp Asp Asp Lys Leu Ala Gln Gln
         1               5                  10

gcc tgc tcc cgt ggg gcc tgc tat cca cct gtt ggg gac ctg ctt gtt    96
Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp Leu Leu Val
 15                  20                  25                  30

ggg agg acc cgg ttt ctc cga gct tca tct acc tgt gga ctg acc aag   144
Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly Leu Thr Lys
                35                  40                  45

cct gag acc tac tgc acc cag tat ggc gag tgg cag atg aaa tgc tgc   192
Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met Lys Cys Cys
            50                  55                  60

aag tgt gac tcc agg cag cct cac aac tac tac agt cac cga gta gag   240
Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His Arg Val Glu
        65                  70                  75

aat gtg gct tca tcc tcc ggc ccc atg cgc tgg tgg cag tcc cag aat   288
Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln Ser Gln Asn
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     80                  85                  90

gat gtg aac cct gtc tct ctg cag ctg gac ctg gac agg aga ttc cag   336
Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg Arg Phe Gln
 95                  100                 105                 110

ctt caa gaa gtc atg atg gag ttc cag ggg ccc atg cct gcc ggc atg   384
Leu Gln Glu Val Met Met Glu Phe Gln Gly Pro Met Pro Ala Gly Met
                115                 120                 125

ctg att gag cgc tcc tca gac ttc ggt aag acc tgg cga gtg tac cag   432
Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg Val Tyr Gln
            130                 135                 140

tac ctg gct gcc gac tgc acc tcc acc ttc cct cgg gtc cgc cag ggt   480
Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val Arg Gln Gly
        145                 150                 155

cgg cct cag agc tgg cag gat gtt cgg tgc cag tcc ctg cct cag agg   528
Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu Pro Gln Arg
    160                 165                 170

cct aat gca cgc cta aat ggg ggg aag gtc caa ctt aac ctt atg gat   576
Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn Leu Met Asp
175                 180                 185                 190

tta gtg tct ggg att cca gca act caa agt caa aaa att caa gag gtg   624
Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln Glu Val
                195                 200                 205

ggg gag atc aca aac ttg aga gtc aat ttc acc agg ctg gcc cct gtg   672
Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu Ala Pro Val
            210                 215                 220

ccc caa agg ggc tac cac cct ccc agc gcc tac tat gct gtg tcc cag   720
Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val Ser Gln
        225                 230                 235

ctc cgt ctg cag ggg agc tgc ttc tgt cac ggc cat gct gat cgc tgc   768
Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala Asp Arg Cys
    240                 245                 250

gca ccc aag cct ggg gcc tct gca ggc ccc tcc acc gct gtg cag gtc   816
Ala Pro Lys Pro Gly Ala Ser Ala Gly Pro Ser Thr Ala Val Gln Val
255                 260                 265                 270

cac gat gtc tgc gtc tgc cag cac aac act gcc ggc cca aat tgt gag   864
His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn Cys Glu
                275                 280                 285

cgc tgt gca ccc ttc tac aac aac cgg ccc tgg aga ccg gcg gag ggc   912
Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala Glu Gly
            290                 295                 300

cag gac gcc cat gaa tgc caa agg tgc gac tgc aat ggg cac tca gag   960
Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His Ser Glu
        305                 310                 315

aca tgt cac ttt gac ccc gct gtg ttt gcc gcc agc cag ggg gca tat  1008
Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly Ala Tyr
    320                 325                 330
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gga ggt gtg tgt gac aat tgc cgg gac cac acc gaa ggc aag aac tgt   1056
Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys Asn Cys
335                 340                 345                 350

gag cgg tgt cag ctg cac tat ttc cgg aac cgg cgc ccg gga gct tcc   1104
Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly Ala Ser
                355                 360                 365

att cag gag acc tgc atc tcc tgc gag tgt gat ccg gat ggg gca gtg   1152
Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly Ala Val
            370                 375                 380

cca ggg gct ccc tgt gac cca gtg acc ggg cag tgt gtg tgc aag gag   1200
Pro Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys Lys Glu
        385                 390                 395

cat gtg cag gga gag cgc tgt gac cta tgc aag ccg ggc ttc act gga   1248
His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe Thr Gly
    400                 405                 410

ctc acc tac gcc aac ccg cag ggc tgc cac cgc tgt gac tgc aac atc   1296
Leu Thr Tyr Ala Asn Pro Gln Gly Cys His Arg Cys Asp Cys Asn Ile
415                 420                 425                 430

ctg ggg tcc cgg agg gac atg ccg tgt gac gag gag agt ggg cgc tgc   1344
Leu Gly Ser Arg Arg Asp Met Pro Cys Asp Glu Glu Ser Gly Arg Cys
                435                 440                 445

ctt tgt ctg ccc aac gtg gtg ggt ccc aaa tgt gac cag tgt gct ccc   1392
Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala Pro
            450                 455                 460

tac cac tgg aag ctg gcc agt ggc cag ggc tgt gaa ccg tgt gcc tgc   1440
Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala Cys
        465                 470                 475

gac ccg cac aac tcc ctc agc cca cag tgc aac cag ttc aca ggg cag   1488
Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly Gln
    480                 485                 490

tgc ccc tgt cgg gaa ggc ttt ggt ggc ctg atg tgc agc gct gca gcc   1536
Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala Ala
495                 500                 505                 510

atc cgc cag tgt cca gac cgg acc tat gga gac gtg gcc aca gga tgc   1584
Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly Cys
                515                 520                 525

cga gcc tgt gac tgt gat ttc cgg gga aca gag ggc ccg ggc tgc gac   1632
Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys Asp
            530                 535                 540

aag gca tca ggc cgc tgc ctc tgc cgc cct ggc ttg acc ggg ccc cgc   1680
Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro Arg
        545                 550                 555

tgt gac cag tgc cag cga ggc tac tgc aat cgc tac ccg gtg tgc gtg   1728
Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val Cys Val
    560                 565                 570
```

```
gcc tgc cac cct tgc ttc cag acc tat gat gcg gac ctc cgg gag cag   1776
Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg Glu Gln
575                 580                 585                 590

gcc ctg cgc ttt ggt aga ctc cgg aat gcc acc gcc agc ctg tgg tca   1824
Ala Leu Arg Phe Gly Arg Leu Arg Asn Ala Thr Ala Ser Leu Trp Ser
                595                 600                 605

ggg cct ggg ctg gag gac cgt ggc ctg gcc tcc cgg atc cta gat gca   1872
Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu Asp Ala
            610                 615                 620

aag agt aag att gag cag atc cga gca gtt ctc agc agc ccc gca gtc   1920
Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro Ala Val
        625                 630                 635

aca gag cag gag gtg gct cag gtg gcc agt gcc atc ctc tcc ctc agg   1968
Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser Leu Arg
    640                 645                 650

cga act ctc cag ggc ctg cag ctg gat ctg ccc ctg gag gag gag acg   2016
Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu Glu Thr
655                 660                 665                 670

ttg tcc ctt ccg aga gac ctg gag agt ctt gac aga agc ttc aat ggt   2064
Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe Asn Gly
                675                 680                 685

ctc ctt act atg tat cag agg aag agg gag cag ttt gaa aaa ata agc   2112
Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys Ile Ser
            690                 695                 700

agt gct gat cct tca gga gcc ttc cgg atg ctg agc aca gcc tac gag   2160
Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala Tyr Glu
        705                 710                 715

cag tca gcc cag gct gct cag cag gtc tcc gac agc tcg cgc ctt ttg   2208
Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg Leu Leu
    720                 725                 730

gac cag ctc agg gac agc cgg aga gag gca gag agg ctg gtg cgg cag   2256
Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val Arg Gln
735                 740                 745                 750

gcg gga gga gga gga ggc acc ggc agc ccc aag ctt gtg gcc ctg agg   2304
Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala Leu Arg
                755                 760                 765

ctg gag atg tct tcg ttg cct gac ctg aca ccc acc ttc aac aag ctc   2352
Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn Lys Leu
            770                 775                 780

tgt ggc aac tcc agg cag atg gct tgc acc cca ata tca tgc cct ggt   2400
Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys Pro Gly
        785                 790                 795

gag cta tgt ccc caa gac aat ggc aca gcc tgt ggc tcc cgc tgc agg   2448
Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Gly Ser Arg Cys Arg
    800                 805                 810

ggt gtc ctt ccc agg gcc ggt ggg gcc ttc ttg atg gcg ggg cag gtg   2496
```

```
Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln Val
815                 820                 825                 830

gct gag cag ctg cgg ggc ttc aat gcc cag ctc cag cgg acc agg cag   2544
Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg Gln
                835                 840                 845

atg att agg gca gcc gag gaa tct gcc tca cag att caa tcc agt gcc   2592
Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser Ala
            850                 855                 860

cag cgc ttg gag acc cag gtg agc gcc agc cgc tcc cag atg gag gaa   2640
Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu Glu
        865                 870                 875

gat gtc aga cgc aca cgg ctc cta atc cag cag gtc cgg gac ttc cta   2688
Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe Leu
    880                 885                 890

aca gac ccc gac act gat gca gcc act atc cag gag gtc agc gag gcc   2736
Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu Ala
895                 900                 905                 910

gtg ctg gcc ctg tgg ctg ccc aca gac tca gct act gtt ctg cag aag   2784
Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln Lys
                915                 920                 925

atg aat gag atc cag gcc att gca gcc agg ctc ccc aac gtg gac ttg   2832
Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp Leu
            930                 935                 940

gtg ctg tcc cag acc aag cag gac att gcg cgt gcc cgc cgg ttg cag   2880
Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu Gln
        945                 950                 955

gct gag gct gag gaa gcc agg agc cga gcc cat gca gtg gag ggc cag   2928
Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly Gln
    960                 965                 970

gtg gaa gat gtg gtt ggg aac ctg cgg cag ggg aca gtg gca ctg cag   2976
Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu Gln
975                 980                 985                 990

gaa gct cag gac acc atg caa ggc acc agc cgc tcc ctt cgg ctt atc   3024
Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu Ile
                995                1000                1005

cag gac agg gtt gct gag gtt cag cag gta ctg cgg cca gca gaa aag   3072
Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu Lys
            1010                1015                1020

ctg gtg aca agc atg acc aag cag ctg ggt gac ttc tgg aca cgg atg   3120
Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg Met
        1025                1030                1035

gag gag ctc cgc cac caa gcc cgg cag cag ggg gca gag gca gtc cag   3168
Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val Gln
    1040                1045                1050

gcc cag cag ctt gcg gaa ggt gcc agc gag cag gca ttg agt gcc caa   3216
Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala Gln
```

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1055                1060                1065                1070

gag gga ttt gag aga ata aaa caa aag tat gct gag ttg aag gac cgg   3264
Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp Arg
                1075                1080                1085

ttg ggt cag agt tcc atg ctg ggt gag cag ggt gcc cgg atc cag agt   3312
Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln Ser
            1090                1095                1100

gtg aag aca gag gca gag gag ctg ttt ggg gag acc atg gag atg atg   3360
Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met Met
        1105                1110                1115

gac agg atg aaa gac atg gag ttg gag ctg ctg cgg ggc agc cag gcc   3408
Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser Gln Ala
    1120                1125                1130

atc atg ctg cgc tca gcg gac ctg aca gga ctg gag aag cgt gtg gag   3456
Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg Val Glu
1135                1140                1145                1150

cag atc cgt gac cac atc aat ggg cgc gtg ctc tac tat gcc acc tgc   3504
Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala Thr Cys
                1155                1160                1165

aag tgat                                                          3511
Lys
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<210> 20
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<212> PRT
<213> Homo sapiens

<400> 20

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Leu Ala Asp Tyr Lys Asp Asp Asp Asp Lys Leu Ala Gln Gln Ala Cys
  1               5                  10                  15

Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp Leu Leu Val Gly Arg
            20                  25                  30

Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly Leu Thr Lys Pro Glu
        35                  40                  45

Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met Lys Cys Cys Lys Cys
    50                  55                  60

Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His Arg Val Glu Asn Val
65                  70                  75                  80

Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln Ser Gln Asn Asp Val
                85                  90                  95

Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg Arg Phe Gln Leu Gln
            100                 105                 110

Glu Val Met Met Glu Phe Gln Gly Pro Met Pro Ala Gly Met Leu Ile
        115                 120                 125

Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg Val Tyr Gln Tyr Leu
```

```
    130                 135                 140

Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val Arg Gln Gly Arg Pro
145                 150                 155                 160

Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu Pro Gln Arg Pro Asn
                165                 170                 175

Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn Leu Met Asp Leu Val
            180                 185                 190

Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln Glu Val Gly Glu
        195                 200                 205

Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu Ala Pro Val Pro Gln
    210                 215                 220

Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val Ser Gln Leu Arg
225                 230                 235                 240

Leu Gln Gly Ser Cys Phe Cys His Gly His Ala Asp Arg Cys Ala Pro
                245                 250                 255

Lys Pro Gly Ala Ser Ala Gly Pro Ser Thr Ala Val Gln Val His Asp
            260                 265                 270

Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn Cys Glu Arg Cys
        275                 280                 285

Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala Glu Gly Gln Asp
    290                 295                 300

Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His Ser Glu Thr Cys
305                 310                 315                 320

His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly Ala Tyr Gly Gly
                325                 330                 335

Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys Asn Cys Glu Arg
            340                 345                 350

Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly Ala Ser Ile Gln
        355                 360                 365

Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly Ala Val Pro Gly
    370                 375                 380

Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys Lys Glu His Val
385                 390                 395                 400

Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe Thr Gly Leu Thr
                405                 410                 415

Tyr Ala Asn Pro Gln Gly Cys His Arg Cys Asp Cys Asn Ile Leu Gly
            420                 425                 430

Ser Arg Arg Asp Met Pro Cys Asp Glu Glu Ser Gly Arg Cys Leu Cys
        435                 440                 445

Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys Ala Pro Tyr His
    450                 455                 460
```

```
Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys Ala Cys Asp Pro
465                 470                 475                 480

His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr Gly Gln Cys Pro
                485                 490                 495

Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala Ala Ala Ile Arg
            500                 505                 510

Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr Gly Cys Arg Ala
        515                 520                 525

Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly Cys Asp Lys Ala
    530                 535                 540

Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly Pro Arg Cys Asp
545                 550                 555                 560

Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val Cys Val Ala Cys
                565                 570                 575

His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg Glu Gln Ala Leu
            580                 585                 590

Arg Phe Gly Arg Leu Arg Asn Ala Thr Ala Ser Leu Trp Ser Gly Pro
        595                 600                 605

Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu Asp Ala Lys Ser
    610                 615                 620

Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro Ala Val Thr Glu
625                 630                 635                 640

Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser Leu Arg Arg Thr
                645                 650                 655

Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu Glu Thr Leu Ser
            660                 665                 670

Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe Asn Gly Leu Leu
        675                 680                 685

Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys Ile Ser Ser Ala
    690                 695                 700

Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala Tyr Glu Gln Ser
705                 710                 715                 720

Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg Leu Leu Asp Gln
                725                 730                 735

Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val Arg Gln Ala Gly
            740                 745                 750

Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala Leu Arg Leu Glu
        755                 760                 765

Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn Lys Leu Cys Gly
    770                 775                 780
```

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Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys Pro Gly Glu Leu
785                 790                 795                 800

Cys Pro Gln Asp Asn Gly Thr Ala Cys Gly Ser Arg Cys Arg Gly Val
                805                 810                 815

Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly Gln Val Ala Glu
            820                 825                 830

Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr Arg Gln Met Ile
        835                 840                 845

Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser Ser Ala Gln Arg
    850                 855                 860

Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met Glu Glu Asp Val
865                 870                 875                 880

Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp Phe Leu Thr Asp
                885                 890                 895

Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser Glu Ala Val Leu
            900                 905                 910

Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu Gln Lys Met Asn
        915                 920                 925

Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val Asp Leu Val Leu
    930                 935                 940

Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg Leu Gln Ala Glu
945                 950                 955                 960

Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu Gly Gln Val Glu
                965                 970                 975

Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala Leu Gln Glu Ala
            980                 985                 990

Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg Leu Ile Gln Asp
        995                1000                1005

Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala Glu Lys Leu Val
   1010                1015                1020

Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr Arg Met Glu Glu
025                1030                1035                1040

Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala Val Gln Ala Gln
               1045                1050                1055

Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser Ala Gln Glu Gly
           1060                1065                1070

Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys Asp Arg Leu Gly
       1075                1080                1085

Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile Gln Ser Val Lys
   1090                1095                1100

Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu Met Met Asp Arg
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105                 1110                1115                1120

Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser Gln Ala Ile Met
                1125                1130                1135

Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg Val Glu Gln Ile
            1140                1145                1150

Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala Thr Cys Lys
        1155                1160                1165


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atg agg gcc tgg atc ttc ttt ctc ctt tgc ctg gcc ggg agg gct ctg  107
Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu
  1               5                  10                  15

gca gcc cca caa caa gcc tgc tcc cgt ggg gcc tgc tat cca cct gtt  155
Ala Ala Pro Gln Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val
             20                  25                  30

ggg gac ctg ctt gtt ggg agg acc cgg ttt ctc cga gct tca tct acc  203
Gly Asp Leu Leu Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr
         35                  40                  45

tgt gga ctg acc aag cct gag acc tac tgc acc cag tat ggc gag tgg  251
Cys Gly Leu Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp
     50                  55                  60

cag atg aaa tgc tgc aag tgt gac tcc agg cag cct cac aac tac tac  299
Gln Met Lys Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr
 65                  70                  75                  80

agt cac cga gta gag aat gtg gct tca tcc tcc ggc ccc atg cgc tgg  347
Ser His Arg Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp
                 85                  90                  95

tgg cag tcc cag aat gat gtg aac cct gtc tct ctg cag ctg gac ctg  395
Trp Gln Ser Gln Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu
            100                 105                 110

gac agg aga ttc cag ctt caa gaa gtc atg atg gag ttc cag ggg ccc  443
Asp Arg Arg Phe Gln Leu Gln Glu Val Met Met Glu Phe Gln Gly Pro
        115                 120                 125

atg cct gcc ggc atg ctg att gag cgc tcc tca gac ttc ggt aag acc  491
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Met Pro Ala Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr
    130                 135                 140

tgg cga gtg tac cag tac ctg gct gcc gac tgc acc tcc acc ttc cct   539
Trp Arg Val Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro
145                 150                 155                 160

cgg gtc cgc cag ggt cgg cct cag agc tgg cag gat gtt cgg tgc cag   587
Arg Val Arg Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln
                165                 170                 175

tcc ctg cct cag agg cct aat gca cgc cta aat ggg ggg aag gtc caa   635
Ser Leu Pro Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln
            180                 185                 190

ctt aac ctt atg gat tta gtg tct ggg att cca gca act caa agt caa   683
Leu Asn Leu Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln
        195                 200                 205

aaa att caa gag gtg ggg gag atc aca aac ttg aga gtc aat ttc acc   731
Lys Ile Gln Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr
    210                 215                 220

agg ctg gcc cct gtg ccc caa agg ggc tac cac cct ccc agc gcc tac   779
Arg Leu Ala Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr
225                 230                 235                 240

tat gct gtg tcc cag ctc cgt ctg cag ggg agc tgc ttc tgt cac ggc   827
Tyr Ala Val Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly
                245                 250                 255

cat gct gat cgc tgc gca ccc aag cct ggg gcc tct gca ggc ccc tcc   875
His Ala Asp Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Pro Ser
            260                 265                 270

acc gct gtg cag gtc cac gat gtc tgc gtc tgc cag cac aac act gcc   923
Thr Ala Val Gln Val His Asp Val Cys Val Cys Gln His Asn Thr Ala
        275                 280                 285

ggc cca aat tgt gag cgc tgt gca ccc ttc tac aac aac cgg ccc tgg   971
Gly Pro Asn Cys Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp
    290                 295                 300

aga ccg gcg gag ggc cag gac gcc cat gaa tgc caa agg tgc gac tgc   1019
Arg Pro Ala Glu Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys
305                 310                 315                 320

aat ggg cac tca gag aca tgt cac ttt gac ccc gct gtg ttt gcc gcc   1067
Asn Gly His Ser Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala
                325                 330                 335

agc cag ggg gca tat gga ggt gtg tgt gac aat tgc cgg gac cac acc   1115
Ser Gln Gly Ala Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr
            340                 345                 350

gaa ggc aag aac tgt gag cgg tgt cag ctg cac tat ttc cgg aac cgg   1163
Glu Gly Lys Asn Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg
        355                 360                 365

cgc ccg gga gct tcc att cag gag acc tgc atc tcc tgc gag tgt gat   1211
Arg Pro Gly Ala Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp
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    370                 375                 380

ccg gat ggg gca gtg cca ggg gct ccc tgt gac cca gtg acc ggg cag   1259
Pro Asp Gly Ala Val Pro Gly Ala Pro Cys Asp Pro Val Thr Gly Gln
385                 390                 395                 400

tgt gtg tgc aag gag cat gtg cag gga gag cgc tgt gac cta tgc aag   1307
Cys Val Cys Lys Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys
                405                 410                 415

ccg ggc ttc act gga ctc acc tac gcc aac ccg cag ggc tgc cac cgc   1355
Pro Gly Phe Thr Gly Leu Thr Tyr Ala Asn Pro Gln Gly Cys His Arg
            420                 425                 430

tgt gac tgc aac atc ctg ggg tcc cgg agg gac atg ccg tgt gac gag   1403
Cys Asp Cys Asn Ile Leu Gly Ser Arg Arg Asp Met Pro Cys Asp Glu
        435                 440                 445

gag agt ggg cgc tgc ctt tgt ctg ccc aac gtg gtg ggt ccc aaa tgt   1451
Glu Ser Gly Arg Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys
    450                 455                 460

gac cag tgt gct ccc tac cac tgg aag ctg gcc agt ggc cag ggc tgt   1499
Asp Gln Cys Ala Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys
465                 470                 475                 480

gaa ccg tgt gcc tgc gac ccg cac aac tcc ctc agc cca cag tgc aac   1547
Glu Pro Cys Ala Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn
                485                 490                 495

cag ttc aca ggg cag tgc ccc tgt cgg gaa ggc ttt ggt ggc ctg atg   1595
Gln Phe Thr Gly Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met
            500                 505                 510

tgc agc gct gca gcc atc cgc cag tgt cca gac cgg acc tat gga gac   1643
Cys Ser Ala Ala Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp
        515                 520                 525

gtg gcc aca gga tgc cga gcc tgt gac tgt gat ttc cgg gga aca gag   1691
Val Ala Thr Gly Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu
    530                 535                 540

ggc ccg ggc tgc gac aag gca tca ggc cgc tgc ctc tgc cgc cct ggc   1739
Gly Pro Gly Cys Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly
545                 550                 555                 560

ttg acc ggg ccc cgc tgt gac cag tgc cag cga ggc tac tgc aat cgc   1787
Leu Thr Gly Pro Arg Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg
                565                 570                 575

tac ccg gtg tgc gtg gcc tgc cac cct tgc ttc cag acc tat gat gcg   1835
Tyr Pro Val Cys Val Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala
            580                 585                 590

gac ctc cgg gag cag gcc ctg cgc ttt ggt aga ctc cgg aat gcc acc   1883
Asp Leu Arg Glu Gln Ala Leu Arg Phe Gly Arg Leu Arg Asn Ala Thr
        595                 600                 605

gcc agc ctg tgg tca ggg cct ggg ctg gag gac cgt ggc ctg gcc tcc   1931
Ala Ser Leu Trp Ser Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser
    610                 615                 620
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cgg atc cta gat gca aag agt aag att gag cag atc cga gca gtt ctc   1979
Arg Ile Leu Asp Ala Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu
625                 630                 635                 640

agc agc ccc gca gtc aca gag cag gag gtg gct cag gtg gcc agt gcc   2027
Ser Ser Pro Ala Val Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala
                645                 650                 655

atc ctc tcc ctc agg cga act ctc cag ggc ctg cag ctg gat ctg ccc   2075
Ile Leu Ser Leu Arg Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro
            660                 665                 670

ctg gag gag gag acg ttg tcc ctt ccg aga gac ctg gag agt ctt gac   2123
Leu Glu Glu Glu Thr Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp
        675                 680                 685

aga agc ttc aat ggt ctc ctt act atg tat cag agg aag agg gag cag   2171
Arg Ser Phe Asn Gly Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln
    690                 695                 700

ttt gaa aaa ata agc agt gct gat cct tca gga gcc ttc cgg atg ctg   2219
Phe Glu Lys Ile Ser Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu
705                 710                 715                 720

agc aca gcc tac gag cag tca gcc cag gct gct cag cag gtc tcc gac   2267
Ser Thr Ala Tyr Glu Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp
                725                 730                 735

agc tcg cgc ctt ttg gac cag ctc agg gac agc cgg aga gag gca gag   2315
Ser Ser Arg Leu Leu Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu
            740                 745                 750

agg ctg gtg cgg cag gcg gga gga gga gga ggc acc ggc agc ccc aag   2363
Arg Leu Val Arg Gln Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys
        755                 760                 765

ctt gtg gcc ctg agg ctg gag atg tct tcg ttg cct gac ctg aca ccc   2411
Leu Val Ala Leu Arg Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro
    770                 775                 780

acc ttc aac aag ctc tgt ggc aac tcc agg cag atg gct tgc acc cca   2459
Thr Phe Asn Lys Leu Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro
785                 790                 795                 800

ata tca tgc cct ggt gag cta tgt ccc caa gac aat ggc aca gcc tgt   2507
Ile Ser Cys Pro Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys
                805                 810                 815

ggc tcc cgc tgc agg ggt gtc ctt ccc agg gcc ggt ggg gcc ttc ttg   2555
Gly Ser Arg Cys Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu
            820                 825                 830

atg gcg ggg cag gtg gct gag cag ctg cgg ggc ttc aat gcc cag ctc   2603
Met Ala Gly Gln Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu
        835                 840                 845

cag cgg acc agg cag atg att agg gca gcc gag gaa tct gcc tca cag   2651
Gln Arg Thr Arg Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln
    850                 855                 860
```

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att caa tcc agt gcc cag cgc ttg gag acc cag gtg agc gcc agc cgc   2699
Ile Gln Ser Ser Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg
865                 870                 875                 880

tcc cag atg gag gaa gat gtc aga cgc aca cgg ctc cta atc cag cag   2747
Ser Gln Met Glu Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln
                885                 890                 895

gtc cgg gac ttc cta aca gac ccc gac act gat gca gcc act atc cag   2795
Val Arg Asp Phe Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln
            900                 905                 910

gag gtc agc gag gcc gtg ctg gcc ctg tgg ctg ccc aca gac tca gct   2843
Glu Val Ser Glu Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala
        915                 920                 925

act gtt ctg cag aag atg aat gag atc cag gcc att gca gcc agg ctc   2891
Thr Val Leu Gln Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu
    930                 935                 940

ccc aac gtg gac ttg gtg ctg tcc cag acc aag cag gac att gcg cgt   2939
Pro Asn Val Asp Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg
945                 950                 955                 960

gcc cgc cgg ttg cag gct gag gct gag gaa gcc agg agc cga gcc cat   2987
Ala Arg Arg Leu Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His
                965                 970                 975

gca gtg gag ggc cag gtg gaa gat gtg gtt ggg aac ctg cgg cag ggg   3035
Ala Val Glu Gly Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly
            980                 985                 990

aca gtg gca ctg cag gaa gct cag gac acc atg caa ggc acc agc cgc   3083
Thr Val Ala Leu Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg
        995                1000                1005

tcc ctt cgg ctt atc cag gac agg gtt gct gag gtt cag cag gta ctg   3131
Ser Leu Arg Leu Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu
   1010                1015                1020

cgg cca gca gaa aag ctg gtg aca agc atg acc aag cag ctg ggt gac   3179
Arg Pro Ala Glu Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp
1025                1030                1035                1040

ttc tgg aca cgg atg gag gag ctc cgc cac caa gcc cgg cag cag ggg   3227
Phe Trp Thr Arg Met Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly
                1045                1050                1055

gca gag gca gtc cag gcc cag cag ctt gcg gaa ggt gcc agc gag cag   3275
Ala Glu Ala Val Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln
            1060                1065                1070

gca ttg agt gcc caa gag gga ttt gag aga ata aaa caa aag tat gct   3323
Ala Leu Ser Ala Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala
        1075                1080                1085

gag ttg aag gac cgg ttg ggt cag agt tcc atg ctg ggt gag cag ggt   3371
Glu Leu Lys Asp Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly
   1090                1095                1100

gcc cgg atc cag agt gtg aag aca gag gca gag gag ctg ttt ggg gag   3419
```

```
Ala Arg Ile Gln Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu
1105                1110                1115                1120

acc atg gag atg atg gac agg atg aaa gac atg gag ttg gag ctg ctg   3467
Thr Met Glu Met Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu
                1125                1130                1135

cgg ggc agc cag gcc atc atg ctg cgc tca gcg gac ctg aca gga ctg   3515
Arg Gly Ser Gln Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu
            1140                1145                1150

gag aag cgt gtg gag cag atc cgt gac cac atc aat ggg cgc gtg ctc   3563
Glu Lys Arg Val Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu
        1155                1160                1165

tac tat gcc acc tgc aag tgat                                     3585
Tyr Tyr Ala Thr Cys Lys
    1170
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<213> Homo sapiens

<400> 22

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Met Arg Ala Trp Ile Phe Phe Leu Leu Cys Leu Ala Gly Arg Ala Leu
  1               5                  10                  15

Ala Ala Pro Gln Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val
             20                  25                  30

Gly Asp Leu Leu Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr
         35                  40                  45

Cys Gly Leu Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp
     50                  55                  60

Gln Met Lys Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr
 65                  70                  75                  80

Ser His Arg Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp
                 85                  90                  95

Trp Gln Ser Gln Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu
            100                 105                 110

Asp Arg Arg Phe Gln Leu Gln Glu Val Met Met Glu Phe Gln Gly Pro
        115                 120                 125

Met Pro Ala Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr
    130                 135                 140

Trp Arg Val Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro
145                 150                 155                 160

Arg Val Arg Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln
                165                 170                 175

Ser Leu Pro Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln
            180                 185                 190
```

```
Leu Asn Leu Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln
        195                 200                 205

Lys Ile Gln Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr
    210                 215                 220

Arg Leu Ala Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr
225                 230                 235                 240

Tyr Ala Val Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly
                245                 250                 255

His Ala Asp Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Pro Ser
            260                 265                 270

Thr Ala Val Gln Val His Asp Val Cys Val Cys Gln His Asn Thr Ala
        275                 280                 285

Gly Pro Asn Cys Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp
    290                 295                 300

Arg Pro Ala Glu Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys
305                 310                 315                 320

Asn Gly His Ser Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala
                325                 330                 335

Ser Gln Gly Ala Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr
            340                 345                 350

Glu Gly Lys Asn Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg
        355                 360                 365

Arg Pro Gly Ala Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp
    370                 375                 380

Pro Asp Gly Ala Val Pro Gly Ala Pro Cys Asp Pro Val Thr Gly Gln
385                 390                 395                 400

Cys Val Cys Lys Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys
                405                 410                 415

Pro Gly Phe Thr Gly Leu Thr Tyr Ala Asn Pro Gln Gly Cys His Arg
            420                 425                 430

Cys Asp Cys Asn Ile Leu Gly Ser Arg Arg Asp Met Pro Cys Asp Glu
        435                 440                 445

Glu Ser Gly Arg Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys
    450                 455                 460

Asp Gln Cys Ala Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys
465                 470                 475                 480

Glu Pro Cys Ala Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn
                485                 490                 495

Gln Phe Thr Gly Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met
            500                 505                 510
```

```
Cys Ser Ala Ala Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp
        515                 520                 525

Val Ala Thr Gly Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu
    530                 535                 540

Gly Pro Gly Cys Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly
545                 550                 555                 560

Leu Thr Gly Pro Arg Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg
                565                 570                 575

Tyr Pro Val Cys Val Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala
            580                 585                 590

Asp Leu Arg Glu Gln Ala Leu Arg Phe Gly Arg Leu Arg Asn Ala Thr
        595                 600                 605

Ala Ser Leu Trp Ser Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser
    610                 615                 620

Arg Ile Leu Asp Ala Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu
625                 630                 635                 640

Ser Ser Pro Ala Val Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala
                645                 650                 655

Ile Leu Ser Leu Arg Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro
            660                 665                 670

Leu Glu Glu Glu Thr Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp
        675                 680                 685

Arg Ser Phe Asn Gly Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln
    690                 695                 700

Phe Glu Lys Ile Ser Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu
705                 710                 715                 720

Ser Thr Ala Tyr Glu Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp
                725                 730                 735

Ser Ser Arg Leu Leu Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu
            740                 745                 750

Arg Leu Val Arg Gln Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys
        755                 760                 765

Leu Val Ala Leu Arg Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro
    770                 775                 780

Thr Phe Asn Lys Leu Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro
785                 790                 795                 800

Ile Ser Cys Pro Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys
                805                 810                 815

Gly Ser Arg Cys Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu
            820                 825                 830

Met Ala Gly Gln Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu
```

```
        835                 840                 845

Gln Arg Thr Arg Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln
    850                 855                 860

Ile Gln Ser Ser Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg
865                 870                 875                 880

Ser Gln Met Glu Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln
                885                 890                 895

Val Arg Asp Phe Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln
            900                 905                 910

Glu Val Ser Glu Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala
        915                 920                 925

Thr Val Leu Gln Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu
    930                 935                 940

Pro Asn Val Asp Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg
945                 950                 955                 960

Ala Arg Arg Leu Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His
                965                 970                 975

Ala Val Glu Gly Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly
            980                 985                 990

Thr Val Ala Leu Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg
        995                1000                1005

Ser Leu Arg Leu Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu
   1010                1015                1020

Arg Pro Ala Glu Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp
1025                1030                1035                1040

Phe Trp Thr Arg Met Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly
                1045                1050                1055

Ala Glu Ala Val Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln
           1060                1065                1070

Ala Leu Ser Ala Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala
       1075                1080                1085

Glu Leu Lys Asp Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly
   1090                1095                1100

Ala Arg Ile Gln Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu
1105                1110                1115                1120

Thr Met Glu Met Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu
                1125                1130                1135

Arg Gly Ser Gln Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu
           1140                1145                1150

Glu Lys Arg Val Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu
       1155                1160                1165
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Tyr Tyr Ala Thr Cys Lys
   1170


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<400> 23
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Gln Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp Leu
  1               5                  10                  15

ctt gtt ggg agg acc cgg ttt ctc cga gct tca tct acc tgt gga ctg   96
Leu Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly Leu
            20                  25                  30

acc aag cct gag acc tac tgc acc cag tat ggc gag tgg cag atg aaa   144
Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met Lys
        35                  40                  45

tgc tgc aag tgt gac tcc agg cag cct cac aac tac tac agt cac cga   192
Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His Arg
    50                  55                  60

gta gag aat gtg gct tca tcc tcc ggc ccc atg cgc tgg tgg cag tcc   240
Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln Ser
65                  70                  75                  80

cag aat gat gtg aac cct gtc tct ctg cag ctg gac ctg gac agg aga   288
Gln Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg Arg
                85                  90                  95

ttc cag ctt caa gaa gtc atg atg gag ttc cag ggg ccc atg cct gcc   336
Phe Gln Leu Gln Glu Val Met Met Glu Phe Gln Gly Pro Met Pro Ala
            100                 105                 110

ggc atg ctg att gag cgc tcc tca gac ttc ggt aag acc tgg cga gtg   384
Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg Val
        115                 120                 125

tac cag tac ctg gct gcc gac tgc acc tcc acc ttc cct cgg gtc cgc   432
Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val Arg
    130                 135                 140

cag ggt cgg cct cag agc tgg cag gat gtt cgg tgc cag tcc ctg cct   480
Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu Pro
145                 150                 155                 160

cag agg cct aat gca cgc cta aat ggg ggg aag gtc caa ctt aac ctt   528
Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn Leu
                165                 170                 175

atg gat tta gtg tct ggg att cca gca act caa agt caa aaa att caa   576
Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln
```

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            180                 185                 190

gag gtg ggg gag atc aca aac ttg aga gtc aat ttc acc agg ctg gcc   624
Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu Ala
        195                 200                 205

cct gtg ccc caa agg ggc tac cac cct ccc agc gcc tac tat gct gtg   672
Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val
    210                 215                 220

tcc cag ctc cgt ctg cag ggg agc tgc ttc tgt cac ggc cat gct gat   720
Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala Asp
225                 230                 235                 240

cgc tgc gca ccc aag cct ggg gcc tct gca ggc ccc tcc acc gct gtg   768
Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Pro Ser Thr Ala Val
                245                 250                 255

cag gtc cac gat gtc tgc gtc tgc cag cac aac act gcc ggc cca aat   816
Gln Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn
            260                 265                 270

tgt gag cgc tgt gca ccc ttc tac aac aac cgg ccc tgg aga ccg gcg   864
Cys Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala
        275                 280                 285

gag ggc cag gac gcc cat gaa tgc caa agg tgc gac tgc aat ggg cac   912
Glu Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His
    290                 295                 300

tca gag aca tgt cac ttt gac ccc gct gtg ttt gcc gcc agc cag ggg   960
Ser Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly
305                 310                 315                 320

gca tat gga ggt gtg tgt gac aat tgc cgg gac cac acc gaa ggc aag   1008
Ala Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys
                325                 330                 335

aac tgt gag cgg tgt cag ctg cac tat ttc cgg aac cgg cgc ccg gga   1056
Asn Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly
            340                 345                 350

gct tcc att cag gag acc tgc atc tcc tgc gag tgt gat ccg gat ggg   1104
Ala Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly
        355                 360                 365

gca gtg cca ggg gct ccc tgt gac cca gtg acc ggg cag tgt gtg tgc   1152
Ala Val Pro Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys
    370                 375                 380

aag gag cat gtg cag gga gag cgc tgt gac cta tgc aag ccg ggc ttc   1200
Lys Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe
385                 390                 395                 400

act gga ctc acc tac gcc aac ccg cag ggc tgc cac cgc tgt gac tgc   1248
Thr Gly Leu Thr Tyr Ala Asn Pro Gln Gly Cys His Arg Cys Asp Cys
                405                 410                 415

aac atc ctg ggg tcc cgg agg gac atg ccg tgt gac gag gag agt ggg   1296
Asn Ile Leu Gly Ser Arg Arg Asp Met Pro Cys Asp Glu Glu Ser Gly
            420                 425                 430
```

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cgc tgc ctt tgt ctg ccc aac gtg gtg ggt ccc aaa tgt gac cag tgt   1344
Arg Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys
        435                 440                 445

gct ccc tac cac tgg aag ctg gcc agt ggc cag ggc tgt gaa ccg tgt   1392
Ala Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys
    450                 455                 460

gcc tgc gac ccg cac aac tcc ctc agc cca cag tgc aac cag ttc aca   1440
Ala Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr
465                 470                 475                 480

ggg cag tgc ccc tgt cgg gaa ggc ttt ggt ggc ctg atg tgc agc gct   1488
Gly Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala
                485                 490                 495

gca gcc atc cgc cag tgt cca gac cgg acc tat gga gac gtg gcc aca   1536
Ala Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr
            500                 505                 510

gga tgc cga gcc tgt gac tgt gat ttc cgg gga aca gag ggc ccg ggc   1584
Gly Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly
        515                 520                 525

tgc gac aag gca tca ggc cgc tgc ctc tgc cgc cct ggc ttg acc ggg   1632
Cys Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly
    530                 535                 540

ccc cgc tgt gac cag tgc cag cga ggc tac tgc aat cgc tac ccg gtg   1680
Pro Arg Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val
545                 550                 555                 560

tgc gtg gcc tgc cac cct tgc ttc cag acc tat gat gcg gac ctc cgg   1728
Cys Val Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg
                565                 570                 575

gag cag gcc ctg cgc ttt ggt aga ctc cgg aat gcc acc gcc agc ctg   1776
Glu Gln Ala Leu Arg Phe Gly Arg Leu Arg Asn Ala Thr Ala Ser Leu
            580                 585                 590

tgg tca ggg cct ggg ctg gag gac cgt ggc ctg gcc tcc cgg atc cta   1824
Trp Ser Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu
        595                 600                 605

gat gca aag agt aag att gag cag atc cga gca gtt ctc agc agc ccc   1872
Asp Ala Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro
    610                 615                 620

gca gtc aca gag cag gag gtg gct cag gtg gcc agt gcc atc ctc tcc   1920
Ala Val Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser
625                 630                 635                 640

ctc agg cga act ctc cag ggc ctg cag ctg gat ctg ccc ctg gag gag   1968
Leu Arg Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu
                645                 650                 655

gag acg ttg tcc ctt ccg aga gac ctg gag agt ctt gac aga agc ttc   2016
Glu Thr Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe
            660                 665                 670
```

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aat ggt ctc ctt act atg tat cag agg aag agg gag cag ttt gaa aaa   2064
Asn Gly Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys
        675                 680                 685

ata agc agt gct gat cct tca gga gcc ttc cgg atg ctg agc aca gcc   2112
Ile Ser Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala
    690                 695                 700

tac gag cag tca gcc cag gct gct cag cag gtc tcc gac agc tcg cgc   2160
Tyr Glu Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg
705                 710                 715                 720

ctt ttg gac cag ctc agg gac agc cgg aga gag gca gag agg ctg gtg   2208
Leu Leu Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val
                725                 730                 735

cgg cag gcg gga gga gga gga ggc acc ggc agc ccc aag ctt gtg gcc   2256
Arg Gln Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala
            740                 745                 750

ctg agg ctg gag atg tct tcg ttg cct gac ctg aca ccc acc ttc aac   2304
Leu Arg Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn
        755                 760                 765

aag ctc tgt ggc aac tcc agg cag atg gct tgc acc cca ata tca tgc   2352
Lys Leu Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys
    770                 775                 780

cct ggt gag cta tgt ccc caa gac aat ggc aca gcc tgt ggc tcc cgc   2400
Pro Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Gly Ser Arg
785                 790                 795                 800

tgc agg ggt gtc ctt ccc agg gcc ggt ggg gcc ttc ttg atg gcg ggg   2448
Cys Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly
                805                 810                 815

cag gtg gct gag cag ctg cgg ggc ttc aat gcc cag ctc cag cgg acc   2496
Gln Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr
            820                 825                 830

agg cag atg att agg gca gcc gag gaa tct gcc tca cag att caa tcc   2544
Arg Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser
        835                 840                 845

agt gcc cag cgc ttg gag acc cag gtg agc gcc agc cgc tcc cag atg   2592
Ser Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met
    850                 855                 860

gag gaa gat gtc aga cgc aca cgg ctc cta atc cag cag gtc cgg gac   2640
Glu Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp
865                 870                 875                 880

ttc cta aca gac ccc gac act gat gca gcc act atc cag gag gtc agc   2688
Phe Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser
                885                 890                 895

gag gcc gtg ctg gcc ctg tgg ctg ccc aca gac tca gct act gtt ctg   2736
Glu Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu
            900                 905                 910

cag aag atg aat gag atc cag gcc att gca gcc agg ctc ccc aac gtg   2784
```

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Gln Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val
        915                 920                 925

gac ttg gtg ctg tcc cag acc aag cag gac att gcg cgt gcc cgc cgg   2832
Asp Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg
    930                 935                 940

ttg cag gct gag gct gag gaa gcc agg agc cga gcc cat gca gtg gag   2880
Leu Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu
945                 950                 955                 960

ggc cag gtg gaa gat gtg gtt ggg aac ctg cgg cag ggg aca gtg gca   2928
Gly Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala
                965                 970                 975

ctg cag gaa gct cag gac acc atg caa ggc acc agc cgc tcc ctt cgg   2976
Leu Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg
            980                 985                 990

ctt atc cag gac agg gtt gct gag gtt cag cag gta ctg cgg cca gca   3024
Leu Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala
        995                 1000                1005

gaa aag ctg gtg aca agc atg acc aag cag ctg ggt gac ttc tgg aca   3072
Glu Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr
   1010                1015                1020

cgg atg gag gag ctc cgc cac caa gcc cgg cag cag ggg gca gag gca   3120
Arg Met Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala
1025                1030                1035                1040

gtc cag gcc cag cag ctt gcg gaa ggt gcc agc gag cag gca ttg agt   3168
Val Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser
               1045                1050                1055

gcc caa gag gga ttt gag aga ata aaa caa aag tat gct gag ttg aag   3216
Ala Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys
           1060                1065                1070

gac cgg ttg ggt cag agt tcc atg ctg ggt gag cag ggt gcc cgg atc   3264
Asp Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile
       1075                1080                1085

cag agt gtg aag aca gag gca gag gag ctg ttt ggg gag acc atg gag   3312
Gln Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu
   1090                1095                1100

atg atg gac agg atg aaa gac atg gag ttg gag ctg ctg cgg ggc agc   3360
Met Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser
1105                1110                1115                1120

cag gcc atc atg ctg cgc tca gcg gac ctg aca gga ctg gag aag cgt   3408
Gln Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg
               1125                1130                1135

gtg gag cag atc cgt gac cac atc aat ggg cgc gtg ctc tac tat gcc   3456
Val Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala
           1140                1145                1150

acc tgc aag tgat                                                 3469
Thr Cys Lys
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1155

<210> 24
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<213> Homo sapiens

<400> 24

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Gln Gln Ala Cys Ser Arg Gly Ala Cys Tyr Pro Pro Val Gly Asp Leu
  1               5                  10                  15

Leu Val Gly Arg Thr Arg Phe Leu Arg Ala Ser Ser Thr Cys Gly Leu
             20                  25                  30

Thr Lys Pro Glu Thr Tyr Cys Thr Gln Tyr Gly Glu Trp Gln Met Lys
         35                  40                  45

Cys Cys Lys Cys Asp Ser Arg Gln Pro His Asn Tyr Tyr Ser His Arg
     50                  55                  60

Val Glu Asn Val Ala Ser Ser Ser Gly Pro Met Arg Trp Trp Gln Ser
 65                  70                  75                  80

Gln Asn Asp Val Asn Pro Val Ser Leu Gln Leu Asp Leu Asp Arg Arg
                 85                  90                  95

Phe Gln Leu Gln Glu Val Met Met Glu Phe Gln Gly Pro Met Pro Ala
            100                 105                 110

Gly Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Arg Val
        115                 120                 125

Tyr Gln Tyr Leu Ala Ala Asp Cys Thr Ser Thr Phe Pro Arg Val Arg
    130                 135                 140

Gln Gly Arg Pro Gln Ser Trp Gln Asp Val Arg Cys Gln Ser Leu Pro
145                 150                 155                 160

Gln Arg Pro Asn Ala Arg Leu Asn Gly Gly Lys Val Gln Leu Asn Leu
                165                 170                 175

Met Asp Leu Val Ser Gly Ile Pro Ala Thr Gln Ser Gln Lys Ile Gln
            180                 185                 190

Glu Val Gly Glu Ile Thr Asn Leu Arg Val Asn Phe Thr Arg Leu Ala
        195                 200                 205

Pro Val Pro Gln Arg Gly Tyr His Pro Pro Ser Ala Tyr Tyr Ala Val
    210                 215                 220

Ser Gln Leu Arg Leu Gln Gly Ser Cys Phe Cys His Gly His Ala Asp
225                 230                 235                 240

Arg Cys Ala Pro Lys Pro Gly Ala Ser Ala Gly Pro Ser Thr Ala Val
                245                 250                 255

Gln Val His Asp Val Cys Val Cys Gln His Asn Thr Ala Gly Pro Asn
            260                 265                 270

Cys Glu Arg Cys Ala Pro Phe Tyr Asn Asn Arg Pro Trp Arg Pro Ala
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        275                 280                 285

Glu Gly Gln Asp Ala His Glu Cys Gln Arg Cys Asp Cys Asn Gly His
    290                 295                 300

Ser Glu Thr Cys His Phe Asp Pro Ala Val Phe Ala Ala Ser Gln Gly
305                 310                 315                 320

Ala Tyr Gly Gly Val Cys Asp Asn Cys Arg Asp His Thr Glu Gly Lys
                325                 330                 335

Asn Cys Glu Arg Cys Gln Leu His Tyr Phe Arg Asn Arg Arg Pro Gly
            340                 345                 350

Ala Ser Ile Gln Glu Thr Cys Ile Ser Cys Glu Cys Asp Pro Asp Gly
        355                 360                 365

Ala Val Pro Gly Ala Pro Cys Asp Pro Val Thr Gly Gln Cys Val Cys
    370                 375                 380

Lys Glu His Val Gln Gly Glu Arg Cys Asp Leu Cys Lys Pro Gly Phe
385                 390                 395                 400

Thr Gly Leu Thr Tyr Ala Asn Pro Gln Gly Cys His Arg Cys Asp Cys
                405                 410                 415

Asn Ile Leu Gly Ser Arg Arg Asp Met Pro Cys Asp Glu Glu Ser Gly
            420                 425                 430

Arg Cys Leu Cys Leu Pro Asn Val Val Gly Pro Lys Cys Asp Gln Cys
        435                 440                 445

Ala Pro Tyr His Trp Lys Leu Ala Ser Gly Gln Gly Cys Glu Pro Cys
    450                 455                 460

Ala Cys Asp Pro His Asn Ser Leu Ser Pro Gln Cys Asn Gln Phe Thr
465                 470                 475                 480

Gly Gln Cys Pro Cys Arg Glu Gly Phe Gly Gly Leu Met Cys Ser Ala
                485                 490                 495

Ala Ala Ile Arg Gln Cys Pro Asp Arg Thr Tyr Gly Asp Val Ala Thr
            500                 505                 510

Gly Cys Arg Ala Cys Asp Cys Asp Phe Arg Gly Thr Glu Gly Pro Gly
        515                 520                 525

Cys Asp Lys Ala Ser Gly Arg Cys Leu Cys Arg Pro Gly Leu Thr Gly
    530                 535                 540

Pro Arg Cys Asp Gln Cys Gln Arg Gly Tyr Cys Asn Arg Tyr Pro Val
545                 550                 555                 560

Cys Val Ala Cys His Pro Cys Phe Gln Thr Tyr Asp Ala Asp Leu Arg
                565                 570                 575

Glu Gln Ala Leu Arg Phe Gly Arg Leu Arg Asn Ala Thr Ala Ser Leu
            580                 585                 590

Trp Ser Gly Pro Gly Leu Glu Asp Arg Gly Leu Ala Ser Arg Ile Leu
        595                 600                 605
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Asp Ala Lys Ser Lys Ile Glu Gln Ile Arg Ala Val Leu Ser Ser Pro
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Ala Val Thr Glu Gln Glu Val Ala Gln Val Ala Ser Ala Ile Leu Ser
625                 630                 635                 640

Leu Arg Arg Thr Leu Gln Gly Leu Gln Leu Asp Leu Pro Leu Glu Glu
                645                 650                 655

Glu Thr Leu Ser Leu Pro Arg Asp Leu Glu Ser Leu Asp Arg Ser Phe
            660                 665                 670

Asn Gly Leu Leu Thr Met Tyr Gln Arg Lys Arg Glu Gln Phe Glu Lys
        675                 680                 685

Ile Ser Ser Ala Asp Pro Ser Gly Ala Phe Arg Met Leu Ser Thr Ala
    690                 695                 700

Tyr Glu Gln Ser Ala Gln Ala Ala Gln Gln Val Ser Asp Ser Ser Arg
705                 710                 715                 720

Leu Leu Asp Gln Leu Arg Asp Ser Arg Arg Glu Ala Glu Arg Leu Val
                725                 730                 735

Arg Gln Ala Gly Gly Gly Gly Gly Thr Gly Ser Pro Lys Leu Val Ala
            740                 745                 750

Leu Arg Leu Glu Met Ser Ser Leu Pro Asp Leu Thr Pro Thr Phe Asn
        755                 760                 765

Lys Leu Cys Gly Asn Ser Arg Gln Met Ala Cys Thr Pro Ile Ser Cys
    770                 775                 780

Pro Gly Glu Leu Cys Pro Gln Asp Asn Gly Thr Ala Cys Gly Ser Arg
785                 790                 795                 800

Cys Arg Gly Val Leu Pro Arg Ala Gly Gly Ala Phe Leu Met Ala Gly
                805                 810                 815

Gln Val Ala Glu Gln Leu Arg Gly Phe Asn Ala Gln Leu Gln Arg Thr
            820                 825                 830

Arg Gln Met Ile Arg Ala Ala Glu Glu Ser Ala Ser Gln Ile Gln Ser
        835                 840                 845

Ser Ala Gln Arg Leu Glu Thr Gln Val Ser Ala Ser Arg Ser Gln Met
    850                 855                 860

Glu Glu Asp Val Arg Arg Thr Arg Leu Leu Ile Gln Gln Val Arg Asp
865                 870                 875                 880

Phe Leu Thr Asp Pro Asp Thr Asp Ala Ala Thr Ile Gln Glu Val Ser
                885                 890                 895

Glu Ala Val Leu Ala Leu Trp Leu Pro Thr Asp Ser Ala Thr Val Leu
            900                 905                 910

Gln Lys Met Asn Glu Ile Gln Ala Ile Ala Ala Arg Leu Pro Asn Val
        915                 920                 925
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Asp Leu Val Leu Ser Gln Thr Lys Gln Asp Ile Ala Arg Ala Arg Arg
    930                 935                 940

Leu Gln Ala Glu Ala Glu Glu Ala Arg Ser Arg Ala His Ala Val Glu
945                 950                 955                 960

Gly Gln Val Glu Asp Val Val Gly Asn Leu Arg Gln Gly Thr Val Ala
                965                 970                 975

Leu Gln Glu Ala Gln Asp Thr Met Gln Gly Thr Ser Arg Ser Leu Arg
            980                 985                 990

Leu Ile Gln Asp Arg Val Ala Glu Val Gln Gln Val Leu Arg Pro Ala
        995                1000                1005

Glu Lys Leu Val Thr Ser Met Thr Lys Gln Leu Gly Asp Phe Trp Thr
   1010                1015                1020

Arg Met Glu Glu Leu Arg His Gln Ala Arg Gln Gln Gly Ala Glu Ala
1025                1030                1035                1040

Val Gln Ala Gln Gln Leu Ala Glu Gly Ala Ser Glu Gln Ala Leu Ser
                1045                1050                1055

Ala Gln Glu Gly Phe Glu Arg Ile Lys Gln Lys Tyr Ala Glu Leu Lys
            1060                1065                1070

Asp Arg Leu Gly Gln Ser Ser Met Leu Gly Glu Gln Gly Ala Arg Ile
        1075                1080                1085

Gln Ser Val Lys Thr Glu Ala Glu Glu Leu Phe Gly Glu Thr Met Glu
   1090                1095                1100

Met Met Asp Arg Met Lys Asp Met Glu Leu Glu Leu Leu Arg Gly Ser
1105                1110                1115                1120

Gln Ala Ile Met Leu Arg Ser Ala Asp Leu Thr Gly Leu Glu Lys Arg
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Val Glu Gln Ile Arg Asp His Ile Asn Gly Arg Val Leu Tyr Tyr Ala
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Thr Cys Lys
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atg cct gcg ctc tgg ctg ggc tgc tgc ctc tgc ttc tcg ctc ctc ctg   165
Met Pro Ala Leu Trp Leu Gly Cys Cys Leu Cys Phe Ser Leu Leu Leu
  1               5                  10                  15

ccc gca gcc cgg gcc acc tcc agg agg gaa gtc tgt gat tgc aat ggg   213
Pro Ala Ala Arg Ala Thr Ser Arg Arg Glu Val Cys Asp Cys Asn Gly
             20                  25                  30

aag tcc agg cag tgt atc ttt gat cgg gaa ctt cac aga caa act ggt   261
Lys Ser Arg Gln Cys Ile Phe Asp Arg Glu Leu His Arg Gln Thr Gly
         35                  40                  45

aat gga ttc cgc tgc ctc aac tgc aat gac aac act gat ggc att cac   309
Asn Gly Phe Arg Cys Leu Asn Cys Asn Asp Asn Thr Asp Gly Ile His
     50                  55                  60

tgc gag aag tgc aag aat ggc ttt tac cgg cac aga gaa agg gac cgc   357
Cys Glu Lys Cys Lys Asn Gly Phe Tyr Arg His Arg Glu Arg Asp Arg
 65                  70                  75                  80

tgt ttg ccc tgc aat tgt aac tcc aaa ggt tct ctt agt gct cga tgt   405
Cys Leu Pro Cys Asn Cys Asn Ser Lys Gly Ser Leu Ser Ala Arg Cys
                 85                  90                  95

gac aac tct gga cgg tgc agc tgt aaa cca ggt gtg aca gga gcc aga   453
Asp Asn Ser Gly Arg Cys Ser Cys Lys Pro Gly Val Thr Gly Ala Arg
            100                 105                 110

tgc gac cga tgt ctg cca ggc ttc cac atg ctc acg gat gcg ggg tgc   501
Cys Asp Arg Cys Leu Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys
        115                 120                 125

acc caa gac cag aga ctg cta gac tcc aag tgt gac tgt gac cca gct   549
Thr Gln Asp Gln Arg Leu Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala
    130                 135                 140

ggc atc gca ggg ccc tgt gac gcg ggc cgc tgt gtc tgc aag cca gct   597
Gly Ile Ala Gly Pro Cys Asp Ala Gly Arg Cys Val Cys Lys Pro Ala
145                 150                 155                 160

gtt act gga gaa cgc tgt gat agg tgt cga tca ggt tac tat aat ctg   645
Val Thr Gly Glu Arg Cys Asp Arg Cys Arg Ser Gly Tyr Tyr Asn Leu
                165                 170                 175

gat ggg ggg aac cct gag ggc tgt acc cag tgt ttc tgc tat ggg cat   693
Asp Gly Gly Asn Pro Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His
            180                 185                 190

tca gcc agc tgc cgc agc tct gca gaa tac agt gtc cat aag atc acc   741
Ser Ala Ser Cys Arg Ser Ser Ala Glu Tyr Ser Val His Lys Ile Thr
        195                 200                 205

tct acc ttt cat caa gat gtt gat ggc tgg aag gct gtc caa cga aat   789
Ser Thr Phe His Gln Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn
    210                 215                 220

ggg tct cct gca aag ctc caa tgg tca cag cgc cat caa gat gtg ttt   837
Gly Ser Pro Ala Lys Leu Gln Trp Ser Gln Arg His Gln Asp Val Ph
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225                 230                 235                 240

agc tca gcc caa cga cta gat cct gtc tat ttt gtg gct cct gcc aaa   885
Ser Ser Ala Gln Arg Leu Asp Pro Val Tyr Phe Val Ala Pro Ala Lys
                245                 250                 255

ttt ctt ggg aat caa cag gtg agc tat ggg caa agc ctg tcc ttt gac   933
Phe Leu Gly Asn Gln Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp
            260                 265                 270

tac cgt gtg gac aga gga ggc aga cac cca tct gcc cat gat gtg atc   981
Tyr Arg Val Asp Arg Gly Gly Arg His Pro Ser Ala His Asp Val Ile
        275                 280                 285

ctg gaa ggt gct ggt cta cgg atc aca gct ccc ttg atg cca ctt ggc   1029
Leu Glu Gly Ala Gly Leu Arg Ile Thr Ala Pro Leu Met Pro Leu Gly
    290                 295                 300

aag aca ctg cct tgt ggg ctc acc aag act tac aca ttc agg tta aat   1077
Lys Thr Leu Pro Cys Gly Leu Thr Lys Thr Tyr Thr Phe Arg Leu Asn
305                 310                 315                 320

gag cat cca agc aat aat tgg agc ccc cag ctg agt tac ttt gag tat   1125
Glu His Pro Ser Asn Asn Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr
                325                 330                 335

cga agg tta ctg cgg aat ctc aca gcc ctc cgc atc cga gct aca tat   1173
Arg Arg Leu Leu Arg Asn Leu Thr Ala Leu Arg Ile Arg Ala Thr Tyr
            340                 345                 350

gga gaa tac agt act ggg tac att gac aat gtg acc ctg att tca gcc   1221
Gly Glu Tyr Ser Thr Gly Tyr Ile Asp Asn Val Thr Leu Ile Ser Ala
        355                 360                 365

cgc cct gtc tct gga gcc cca gca ccc tgg gtt gaa cag tgt ata tgt   1269
Arg Pro Val Ser Gly Ala Pro Ala Pro Trp Val Glu Gln Cys Ile Cys
    370                 375                 380

cct gtt ggg tac aag ggg caa ttc tgc cag gat tgt gct tct ggc tac   1317
Pro Val Gly Tyr Lys Gly Gln Phe Cys Gln Asp Cys Ala Ser Gly Tyr
385                 390                 395                 400

aag aga gat tca gcg aga ctg ggg cct ttt ggc acc tgt att cct tgt   1365
Lys Arg Asp Ser Ala Arg Leu Gly Pro Phe Gly Thr Cys Ile Pro Cys
                405                 410                 415

aac tgt caa ggg gga ggg gcc tgt gat cca gac aca gga gat tgt tat   1413
Asn Cys Gln Gly Gly Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr
            420                 425                 430

tca ggg gat gag aat cct gac att gag tgt gct gac tgc cca att ggt   1461
Ser Gly Asp Glu Asn Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly
        435                 440                 445

ttc tac aac gat ccg cac gac ccc cgc agc tgc aag cca tgt ccc tgt   1509
Phe Tyr Asn Asp Pro His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys
    450                 455                 460

cat aac ggg ttc agc tgc tca gtg att ccg gag acg gag gag gtg gtg   1557
His Asn Gly Phe Ser Cys Ser Val Ile Pro Glu Thr Glu Glu Val Val
465                 470                 475                 480
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tgc aat aac tgc cct ccc ggg gtc acc ggt gcc cgc tgt gag ctc tgt   1605
Cys Asn Asn Cys Pro Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys
                485                 490                 495

gct gat ggc tac ttt ggg gac ccc ttt ggt gaa cat ggc cca gtg agg   1653
Ala Asp Gly Tyr Phe Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg
            500                 505                 510

cct tgt cag ccc tgt caa tgc aac agc aat gtg gac ccc agt gcc tct   1701
Pro Cys Gln Pro Cys Gln Cys Asn Ser Asn Val Asp Pro Ser Ala Ser
        515                 520                 525

ggg aat tgt gac cgg ctg aca ggc agg tgt ttg aag tgt atc cac aac   1749
Gly Asn Cys Asp Arg Leu Thr Gly Arg Cys Leu Lys Cys Ile His Asn
    530                 535                 540

aca gcc ggc atc tac tgc gac cag tgc aaa gca ggc tac ttc ggg gac   1797
Thr Ala Gly Ile Tyr Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp
545                 550                 555                 560

cca ttg gct ccc aac cca gca gac aag tgt cga gct tgc aac tgt aac   1845
Pro Leu Ala Pro Asn Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Asn
                565                 570                 575

ccc atg ggc tca gag cct gta gga tgt cga agt gat ggc acc tgt gtt   1893
Pro Met Gly Ser Glu Pro Val Gly Cys Arg Ser Asp Gly Thr Cys Val
            580                 585                 590

tgc aag cca gga ttt ggt ggc ccc aac tgt gag cat gga gca ttc agc   1941
Cys Lys Pro Gly Phe Gly Gly Pro Asn Cys Glu His Gly Ala Phe Ser
        595                 600                 605

tgt cca gct tgc tat aat caa gtg aag att cag atg gat cag ttt atg   1989
Cys Pro Ala Cys Tyr Asn Gln Val Lys Ile Gln Met Asp Gln Phe Met
    610                 615                 620

cag cag ctt cag aga atg gag gcc ctg att tca aag gct cag ggt ggt   2037
Gln Gln Leu Gln Arg Met Glu Ala Leu Ile Ser Lys Ala Gln Gly Gly
625                 630                 635                 640

gat gga gta gta cct gat aca gag ctg gaa ggc agg atg cag cag gct   2085
Asp Gly Val Val Pro Asp Thr Glu Leu Glu Gly Arg Met Gln Gln Ala
                645                 650                 655

gag cag gcc ctt cag gac att ctg aga gat gcc cag att tca gaa ggt   2133
Glu Gln Ala Leu Gln Asp Ile Leu Arg Asp Ala Gln Ile Ser Glu Gly
            660                 665                 670

gct agc aga tcc ctt ggt ctc cag ttg gcc aag gtg agg agc caa gag   2181
Ala Ser Arg Ser Leu Gly Leu Gln Leu Ala Lys Val Arg Ser Gln Glu
        675                 680                 685

aac agc tac cag agc cgc ctg gat gac ctc aag atg act gtg gaa aga   2229
Asn Ser Tyr Gln Ser Arg Leu Asp Asp Leu Lys Met Thr Val Glu Arg
    690                 695                 700

gtt cgg gct ctg gga agt cag tac cag aac cga gtt cgg gat act cac   2277
Val Arg Ala Leu Gly Ser Gln Tyr Gln Asn Arg Val Arg Asp Thr His
705                 710                 715                 720
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agg ctc atc act cag atg cag ctg agc ctg gca gaa agt gaa gct tcc   2325
Arg Leu Ile Thr Gln Met Gln Leu Ser Leu Ala Glu Ser Glu Ala Ser
                725                 730                 735

ttg gga aac act aac att cct gcc tca gac cac tac gtg ggg cca aat   2373
Leu Gly Asn Thr Asn Ile Pro Ala Ser Asp His Tyr Val Gly Pro Asn
            740                 745                 750

ggc ttt aaa agt ctg gct cag gag gcc aca aga tta gca gaa agc cac   2421
Gly Phe Lys Ser Leu Ala Gln Glu Ala Thr Arg Leu Ala Glu Ser His
        755                 760                 765

gtt gag tca gcc agt aac atg gag caa ctg aca agg gaa act gag gac   2469
Val Glu Ser Ala Ser Asn Met Glu Gln Leu Thr Arg Glu Thr Glu Asp
    770                 775                 780

tat tcc aaa caa gcc ctc tca ctg gtg cgc aag gcc ctg cat gaa gga   2517
Tyr Ser Lys Gln Ala Leu Ser Leu Val Arg Lys Ala Leu His Glu Gly
785                 790                 795                 800

gtc gga agc gga agc ggt agc ccg gac ggt gct gtg gtg caa ggg ctt   2565
Val Gly Ser Gly Ser Gly Ser Pro Asp Gly Ala Val Val Gln Gly Leu
                805                 810                 815

gtg gaa aaa ttg gag aaa acc aag tcc ctg gcc cag cag ttg aca agg   2613
Val Glu Lys Leu Glu Lys Thr Lys Ser Leu Ala Gln Gln Leu Thr Arg
            820                 825                 830

gag gcc act caa gcg gaa att gaa gca gat agg tct tat cag cac agt   2661
Glu Ala Thr Gln Ala Glu Ile Glu Ala Asp Arg Ser Tyr Gln His Ser
        835                 840                 845

ctc cgc ctc ctg gat tca gtg tct ccg ctt cag gga gtc agt gat cag   2709
Leu Arg Leu Leu Asp Ser Val Ser Pro Leu Gln Gly Val Ser Asp Gln
    850                 855                 860

tcc ttt cag gtg gaa gaa gca aag agg atc aaa caa aaa gcg gat tca   2757
Ser Phe Gln Val Glu Glu Ala Lys Arg Ile Lys Gln Lys Ala Asp Ser
865                 870                 875                 880

ctc tca agc ctg gta acc agg cat atg gat gag ttc aag cgt aca caa   2805
Leu Ser Ser Leu Val Thr Arg His Met Asp Glu Phe Lys Arg Thr Gln
                885                 890                 895

aag aat ctg gga aac tgg aaa gaa gaa gca cag cag ctc tta cag aat   2853
Lys Asn Leu Gly Asn Trp Lys Glu Glu Ala Gln Gln Leu Leu Gln Asn
            900                 905                 910

gga aaa agt ggg aga gag aaa tca gat cag ctg ctt tcc cgt gcc aat   2901
Gly Lys Ser Gly Arg Glu Lys Ser Asp Gln Leu Leu Ser Arg Ala Asn
        915                 920                 925

ctt gct aaa agc aga gca caa gaa gca ctg agt atg ggc aat gcc act   2949
Leu Ala Lys Ser Arg Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr
    930                 935                 940

ttt tat gaa gtt gag agc atc ctt aaa aac ctc aga gag ttt gac ctg   2997
Phe Tyr Glu Val Glu Ser Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu
945                 950                 955                 960

cag gtg gac aac aga aaa gca gaa gct gaa gaa gcc atg aag aga ctc   3045
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Gln Val Asp Asn Arg Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu
                965                 970                 975

tcc tac atc agc cag aag gtt tca gat gcc agt gac aag acc cag caa  3093
Ser Tyr Ile Ser Gln Lys Val Ser Asp Ala Ser Asp Lys Thr Gln Gln
            980                 985                 990

gca gaa aga gcc ctg ggg agc gct gct gct gat gca cag agg gca aag  3141
Ala Glu Arg Ala Leu Gly Ser Ala Ala Ala Asp Ala Gln Arg Ala Lys
        995                1000                1005

aat ggg gcc ggg gag gcc ctg gaa atc tcc agt gag att gaa cag gag  3189
Asn Gly Ala Gly Glu Ala Leu Glu Ile Ser Ser Glu Ile Glu Gln Glu
   1010                1015                1020

att ggg agt ctg aac ttg gaa gcc aat gtg aca gca gat gga gcc ttg  3237
Ile Gly Ser Leu Asn Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu
1025                1030                1035                1040

gcc atg gaa aag gga ctg gcc tct ctg aag agt gag atg agg gaa gtg  3285
Ala Met Glu Lys Gly Leu Ala Ser Leu Lys Ser Glu Met Arg Glu Val
               1045                1050                1055

gaa gga gag ctg gaa agg aag gag ctg gag ttt gac acg aat atg gat  3333
Glu Gly Glu Leu Glu Arg Lys Glu Leu Glu Phe Asp Thr Asn Met Asp
           1060                1065                1070

gca gta cag atg gtg att aca gaa gcc cag aag gtt gat acc aga gcc  3381
Ala Val Gln Met Val Ile Thr Glu Ala Gln Lys Val Asp Thr Arg Ala
       1075                1080                1085

aag aac gct ggg gtt aca atc caa gac aca ctc aac aca tta gac ggc  3429
Lys Asn Ala Gly Val Thr Ile Gln Asp Thr Leu Asn Thr Leu Asp Gly
   1090                1095                1100

ctc ctg cat ctg atg gac cag cct ctc agt gta gat gaa gag ggg ctg  3477
Leu Leu His Leu Met Asp Gln Pro Leu Ser Val Asp Glu Glu Gly Leu
1105                1110                1115                1120

gtc tta ctg gag cag aag ctt tcc cga gcc aag acc cag atc aac agc  3525
Val Leu Leu Glu Gln Lys Leu Ser Arg Ala Lys Thr Gln Ile Asn Ser
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caa ctg cgg ccc atg atg tca gag ctg gaa gag agg gca cgt cag cag  3573
Gln Leu Arg Pro Met Met Ser Glu Leu Glu Glu Arg Ala Arg Gln Gln
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agg ggc cac ctc cat ttg ctg gag aca agc ata gat ggg att ctg gct  3621
Arg Gly His Leu His Leu Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala
       1155                1160                1165

gat gtg aag aac ttg gag aac att agg gac aac ctg ccc cca ggc tgc  3669
Asp Val Lys Asn Leu Glu Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys
   1170                1175                1180

tac aat acc cag gct ctt gag caa cag tgaagctgcc ataaatattt        3716
Tyr Asn Thr Gln Ala Leu Glu Gln Gln
1185                1190

ctcaactgag gttcttggga tacagatctc agggctcggg agccatgtca tgtgagtggg 3776
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Lys Ser Arg Gln Cys Ile Phe Asp Arg Glu Leu His Arg Gln Thr Gly
         35                  40                  45

Asn Gly Phe Arg Cys Leu Asn Cys Asn Asp Asn Thr Asp Gly Ile His
     50                  55                  60

Cys Glu Lys Cys Lys Asn Gly Phe Tyr Arg His Arg Glu Arg Asp Arg
 65                  70                  75                  80

Cys Leu Pro Cys Asn Cys Asn Ser Lys Gly Ser Leu Ser Ala Arg Cys
                 85                  90                  95

Asp Asn Ser Gly Arg Cys Ser Cys Lys Pro Gly Val Thr Gly Ala Arg
            100                 105                 110

Cys Asp Arg Cys Leu Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys
        115                 120                 125

Thr Gln Asp Gln Arg Leu Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala
    130                 135                 140

Gly Ile Ala Gly Pro Cys Asp Ala Gly Arg Cys Val Cys Lys Pro Ala
145                 150                 155                 160

Val Thr Gly Glu Arg Cys Asp Arg Cys Arg Ser Gly Tyr Tyr Asn Leu
                165                 170                 175

Asp Gly Gly Asn Pro Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His
            180                 185                 190

Ser Ala Ser Cys Arg Ser Ser Ala Glu Tyr Ser Val His Lys Ile Thr
        195                 200                 205

Ser Thr Phe His Gln Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn
    210                 215                 220

Gly Ser Pro Ala Lys Leu Gln Trp Ser Gln Arg His Gln Asp Val Phe
225                 230                 235                 240

Ser Ser Ala Gln Arg Leu Asp Pro Val Tyr Phe Val Ala Pro Ala Lys
                245                 250                 255

Phe Leu Gly Asn Gln Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp
            260                 265                 270

Tyr Arg Val Asp Arg Gly Gly Arg His Pro Ser Ala His Asp Val Ile
        275                 280                 285

Leu Glu Gly Ala Gly Leu Arg Ile Thr Ala Pro Leu Met Pro Leu Gly
    290                 295                 300

Lys Thr Leu Pro Cys Gly Leu Thr Lys Thr Tyr Thr Phe Arg Leu Asn
305                 310                 315                 320

Glu His Pro Ser Asn Asn Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr
                325                 330                 335

Arg Arg Leu Leu Arg Asn Leu Thr Ala Leu Arg Ile Arg Ala Thr Tyr
            340                 345                 350

Gly Glu Tyr Ser Thr Gly Tyr Ile Asp Asn Val Thr Leu Ile Ser Ala
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355 360 365

Arg Pro Val Ser Gly Ala Pro Ala Pro Trp Val Glu Gln Cys Ile Cys
370 375 380

Pro Val Gly Tyr Lys Gly Gln Phe Cys Gln Asp Cys Ala Ser Gly Tyr
385 390 395 400

Lys Arg Asp Ser Ala Arg Leu Gly Pro Phe Gly Thr Cys Ile Pro Cys
405 410 415

Asn Cys Gln Gly Gly Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr
420 425 430

Ser Gly Asp Glu Asn Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly
435 440 445

Phe Tyr Asn Asp Pro His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys
450 455 460

His Asn Gly Phe Ser Cys Ser Val Ile Pro Glu Thr Glu Glu Val Val
465 470 475 480

Cys Asn Asn Cys Pro Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys
485 490 495

Ala Asp Gly Tyr Phe Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg
500 505 510

Pro Cys Gln Pro Cys Gln Cys Asn Ser Asn Val Asp Pro Ser Ala Ser
515 520 525

Gly Asn Cys Asp Arg Leu Thr Gly Arg Cys Leu Lys Cys Ile His Asn
530 535 540

Thr Ala Gly Ile Tyr Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp
545 550 555 560

Pro Leu Ala Pro Asn Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Asn
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Pro Met Gly Ser Glu Pro Val Gly Cys Arg Ser Asp Gly Thr Cys Val
580 585 590

Cys Lys Pro Gly Phe Gly Gly Pro Asn Cys Glu His Gly Ala Phe Ser
595 600 605

Cys Pro Ala Cys Tyr Asn Gln Val Lys Ile Gln Met Asp Gln Phe Met
610 615 620

Gln Gln Leu Gln Arg Met Glu Ala Leu Ile Ser Lys Ala Gln Gly Gly
625 630 635 640

Asp Gly Val Val Pro Asp Thr Glu Leu Glu Gly Arg Met Gln Gln Ala
645 650 655

Glu Gln Ala Leu Gln Asp Ile Leu Arg Asp Ala Gln Ile Ser Glu Gly
660 665 670

Ala Ser Arg Ser Leu Gly Leu Gln Leu Ala Lys Val Arg Ser Gln Glu
675 680 685

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Asn Ser Tyr Gln Ser Arg Leu Asp Asp Leu Lys Met Thr Val Glu Arg
    690                 695                 700

Val Arg Ala Leu Gly Ser Gln Tyr Gln Asn Arg Val Arg Asp Thr His
705                 710                 715                 720

Arg Leu Ile Thr Gln Met Gln Leu Ser Leu Ala Glu Ser Glu Ala Ser
                725                 730                 735

Leu Gly Asn Thr Asn Ile Pro Ala Ser Asp His Tyr Val Gly Pro Asn
            740                 745                 750

Gly Phe Lys Ser Leu Ala Gln Glu Ala Thr Arg Leu Ala Glu Ser His
        755                 760                 765

Val Glu Ser Ala Ser Asn Met Glu Gln Leu Thr Arg Glu Thr Glu Asp
    770                 775                 780

Tyr Ser Lys Gln Ala Leu Ser Leu Val Arg Lys Ala Leu His Glu Gly
785                 790                 795                 800

Val Gly Ser Gly Ser Gly Ser Pro Asp Gly Ala Val Val Gln Gly Leu
                805                 810                 815

Val Glu Lys Leu Glu Lys Thr Lys Ser Leu Ala Gln Gln Leu Thr Arg
            820                 825                 830

Glu Ala Thr Gln Ala Glu Ile Glu Ala Asp Arg Ser Tyr Gln His Ser
        835                 840                 845

Leu Arg Leu Leu Asp Ser Val Ser Pro Leu Gln Gly Val Ser Asp Gln
    850                 855                 860

Ser Phe Gln Val Glu Glu Ala Lys Arg Ile Lys Gln Lys Ala Asp Ser
865                 870                 875                 880

Leu Ser Ser Leu Val Thr Arg His Met Asp Glu Phe Lys Arg Thr Gln
                885                 890                 895

Lys Asn Leu Gly Asn Trp Lys Glu Glu Ala Gln Gln Leu Leu Gln Asn
            900                 905                 910

Gly Lys Ser Gly Arg Glu Lys Ser Asp Gln Leu Leu Ser Arg Ala Asn
        915                 920                 925

Leu Ala Lys Ser Arg Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr
    930                 935                 940

Phe Tyr Glu Val Glu Ser Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu
945                 950                 955                 960

Gln Val Asp Asn Arg Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu
                965                 970                 975

Ser Tyr Ile Ser Gln Lys Val Ser Asp Ala Ser Asp Lys Thr Gln Gln
            980                 985                 990

Ala Glu Arg Ala Leu Gly Ser Ala Ala Ala Asp Ala Gln Arg Ala Lys
        995                1000                1005
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Asn Gly Ala Gly Glu Ala Leu Glu Ile Ser Ser Glu Ile Glu Gln Glu
   1010                1015                1020

Ile Gly Ser Leu Asn Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu
1025                1030                1035                1040

Ala Met Glu Lys Gly Leu Ala Ser Leu Lys Ser Glu Met Arg Glu Val
                1045                1050                1055

Glu Gly Glu Leu Glu Arg Lys Glu Leu Glu Phe Asp Thr Asn Met Asp
            1060                1065                1070

Ala Val Gln Met Val Ile Thr Glu Ala Gln Lys Val Asp Thr Arg Ala
        1075                1080                1085

Lys Asn Ala Gly Val Thr Ile Gln Asp Thr Leu Asn Thr Leu Asp Gly
   1090                1095                1100

Leu Leu His Leu Met Asp Gln Pro Leu Ser Val Asp Glu Glu Gly Leu
1105                1110                1115                1120

Val Leu Leu Glu Gln Lys Leu Ser Arg Ala Lys Thr Gln Ile Asn Ser
                1125                1130                1135

Gln Leu Arg Pro Met Met Ser Glu Leu Glu Glu Arg Ala Arg Gln Gln
            1140                1145                1150

Arg Gly His Leu His Leu Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala
        1155                1160                1165

Asp Val Lys Asn Leu Glu Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys
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Tyr Asn Thr Gln Ala Leu Glu Gln Gln
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atc ttt gat cgg gaa ctt cac aga caa act ggt aat gga ttc cgc tgc   96
Ile Phe Asp Arg Glu Leu His Arg Gln Thr Gly Asn Gly Phe Arg Cys
             20                  25                  30

ctc aac tgc aat gac aac act gat ggc att cac tgc gag aag tgc aag   144
Leu Asn Cys Asn Asp Asn Thr Asp Gly Ile His Cys Glu Lys Cys Lys
         35                  40                  45

aat ggc ttt tac cgg cac aga gaa agg gac cgc tgt ttg ccc tgc aat   192
Asn Gly Phe Tyr Arg His Arg Glu Arg Asp Arg Cys Leu Pro Cys Asn
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     50                  55                  60

tgt aac tcc aaa ggt tct ctt agt gct cga tgt gac aac tct gga cgg   240
Cys Asn Ser Lys Gly Ser Leu Ser Ala Arg Cys Asp Asn Ser Gly Arg
 65                  70                  75                  80

tgc agc tgt aaa cca ggt gtg aca gga gcc aga tgc gac cga tgt ctg   288
Cys Ser Cys Lys Pro Gly Val Thr Gly Ala Arg Cys Asp Arg Cys Leu
                 85                  90                  95

cca ggc ttc cac atg ctc acg gat gcg ggg tgc acc caa gac cag aga   336
Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys Thr Gln Asp Gln Arg
            100                 105                 110

ctg cta gac tcc aag tgt gac tgt gac cca gct ggc atc gca ggg ccc   384
Leu Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala Gly Ile Ala Gly Pro
        115                 120                 125

tgt gac gcg ggc cgc tgt gtc tgc aag cca gct gtt act gga gaa cgc   432
Cys Asp Ala Gly Arg Cys Val Cys Lys Pro Ala Val Thr Gly Glu Arg
    130                 135                 140

tgt gat agg tgt cga tca ggt tac tat aat ctg gat ggg ggg aac cct   480
Cys Asp Arg Cys Arg Ser Gly Tyr Tyr Asn Leu Asp Gly Gly Asn Pro
145                 150                 155                 160

gag ggc tgt acc cag tgt ttc tgc tat ggg cat tca gcc agc tgc cgc   528
Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His Ser Ala Ser Cys Arg
                165                 170                 175

agc tct gca gaa tac agt gtc cat aag atc acc tct acc ttt cat caa   576
Ser Ser Ala Glu Tyr Ser Val His Lys Ile Thr Ser Thr Phe His Gln
            180                 185                 190

gat gtt gat ggc tgg aag gct gtc caa cga aat ggg tct cct gca aag   624
Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn Gly Ser Pro Ala Lys
        195                 200                 205

ctc caa tgg tca cag cgc cat caa gat gtg ttt agc tca gcc caa cga   672
Leu Gln Trp Ser Gln Arg His Gln Asp Val Phe Ser Ser Ala Gln Arg
    210                 215                 220

cta gat cct gtc tat ttt gtg gct cct gcc aaa ttt ctt ggg aat caa   720
Leu Asp Pro Val Tyr Phe Val Ala Pro Ala Lys Phe Leu Gly Asn Gln
225                 230                 235                 240

cag gtg agc tat ggg caa agc ctg tcc ttt gac tac cgt gtg gac aga   768
Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp Tyr Arg Val Asp Arg
                245                 250                 255

gga ggc aga cac cca tct gcc cat gat gtg atc ctg gaa ggt gct ggt   816
Gly Gly Arg His Pro Ser Ala His Asp Val Ile Leu Glu Gly Ala Gly
            260                 265                 270

cta cgg atc aca gct ccc ttg atg cca ctt ggc aag aca ctg cct tgt   864
Leu Arg Ile Thr Ala Pro Leu Met Pro Leu Gly Lys Thr Leu Pro Cys
        275                 280                 285

ggg ctc acc aag act tac aca ttc agg tta aat gag cat cca agc aat   912
Gly Leu Thr Lys Thr Tyr Thr Phe Arg Leu Asn Glu His Pro Ser Asn
    290                 295                 300
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aat tgg agc ccc cag ctg agt tac ttt gag tat cga agg tta ctg cgg   960
Asn Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr Arg Arg Leu Leu Arg
305                 310                 315                 320

aat ctc aca gcc ctc cgc atc cga gct aca tat gga gaa tac agt act   1008
Asn Leu Thr Ala Leu Arg Ile Arg Ala Thr Tyr Gly Glu Tyr Ser Thr
                325                 330                 335

ggg tac att gac aat gtg acc ctg att tca gcc cgc cct gtc tct gga   1056
Gly Tyr Ile Asp Asn Val Thr Leu Ile Ser Ala Arg Pro Val Ser Gly
            340                 345                 350

gcc cca gca ccc tgg gtt gaa cag tgt ata tgt cct gtt ggg tac aag   1104
Ala Pro Ala Pro Trp Val Glu Gln Cys Ile Cys Pro Val Gly Tyr Lys
        355                 360                 365

ggg caa ttc tgc cag gat tgt gct tct ggc tac aag aga gat tca gcg   1152
Gly Gln Phe Cys Gln Asp Cys Ala Ser Gly Tyr Lys Arg Asp Ser Ala
    370                 375                 380

aga ctg ggg cct ttt ggc acc tgt att cct tgt aac tgt caa ggg gga   1200
Arg Leu Gly Pro Phe Gly Thr Cys Ile Pro Cys Asn Cys Gln Gly Gly
385                 390                 395                 400

ggg gcc tgt gat cca gac aca gga gat tgt tat tca ggg gat gag aat   1248
Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr Ser Gly Asp Glu Asn
                405                 410                 415

cct gac att gag tgt gct gac tgc cca att ggt ttc tac aac gat ccg   1296
Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly Phe Tyr Asn Asp Pro
            420                 425                 430

cac gac ccc cgc agc tgc aag cca tgt ccc tgt cat aac ggg ttc agc   1344
His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys His Asn Gly Phe Ser
        435                 440                 445

tgc tca gtg att ccg gag acg gag gag gtg gtg tgc aat aac tgc cct   1392
Cys Ser Val Ile Pro Glu Thr Glu Glu Val Val Cys Asn Asn Cys Pro
    450                 455                 460

ccc ggg gtc acc ggt gcc cgc tgt gag ctc tgt gct gat ggc tac ttt   1440
Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys Ala Asp Gly Tyr Phe
465                 470                 475                 480

ggg gac ccc ttt ggt gaa cat ggc cca gtg agg cct tgt cag ccc tgt   1488
Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg Pro Cys Gln Pro Cys
                485                 490                 495

caa tgc aac agc aat gtg gac ccc agt gcc tct ggg aat tgt gac cgg   1536
Gln Cys Asn Ser Asn Val Asp Pro Ser Ala Ser Gly Asn Cys Asp Arg
            500                 505                 510

ctg aca ggc agg tgt ttg aag tgt atc cac aac aca gcc ggc atc tac   1584
Leu Thr Gly Arg Cys Leu Lys Cys Ile His Asn Thr Ala Gly Ile Tyr
        515                 520                 525

tgc gac cag tgc aaa gca ggc tac ttc ggg gac cca ttg gct ccc aac   1632
Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp Pro Leu Ala Pro Asn
    530                 535                 540
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cca gca gac aag tgt cga gct tgc aac tgt aac ccc atg ggc tca gag   1680
Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Asn Pro Met Gly Ser Glu
545                 550                 555                 560

cct gta gga tgt cga agt gat ggc acc tgt gtt tgc aag cca gga ttt   1728
Pro Val Gly Cys Arg Ser Asp Gly Thr Cys Val Cys Lys Pro Gly Phe
                565                 570                 575

ggt ggc ccc aac tgt gag cat gga gca ttc agc tgt cca gct tgc tat   1776
Gly Gly Pro Asn Cys Glu His Gly Ala Phe Ser Cys Pro Ala Cys Tyr
            580                 585                 590

aat caa gtg aag att cag atg gat cag ttt atg cag cag ctt cag aga   1824
Asn Gln Val Lys Ile Gln Met Asp Gln Phe Met Gln Gln Leu Gln Arg
        595                 600                 605

atg gag gcc ctg att tca aag gct cag ggt ggt gat gga gta gta cct   1872
Met Glu Ala Leu Ile Ser Lys Ala Gln Gly Gly Asp Gly Val Val Pro
    610                 615                 620

gat aca gag ctg gaa ggc agg atg cag cag gct gag cag gcc ctt cag   1920
Asp Thr Glu Leu Glu Gly Arg Met Gln Gln Ala Glu Gln Ala Leu Gln
625                 630                 635                 640

gac att ctg aga gat gcc cag att tca gaa ggt gct agc aga tcc ctt   1968
Asp Ile Leu Arg Asp Ala Gln Ile Ser Glu Gly Ala Ser Arg Ser Leu
                645                 650                 655

ggt ctc cag ttg gcc aag gtg agg agc caa gag aac agc tac cag agc   2016
Gly Leu Gln Leu Ala Lys Val Arg Ser Gln Glu Asn Ser Tyr Gln Ser
            660                 665                 670

cgc ctg gat gac ctc aag atg act gtg gaa aga gtt cgg gct ctg gga   2064
Arg Leu Asp Asp Leu Lys Met Thr Val Glu Arg Val Arg Ala Leu Gly
        675                 680                 685

agt cag tac cag aac cga gtt cgg gat act cac agg ctc atc act cag   2112
Ser Gln Tyr Gln Asn Arg Val Arg Asp Thr His Arg Leu Ile Thr Gln
    690                 695                 700

atg cag ctg agc ctg gca gaa agt gaa gct tcc ttg gga aac act aac   2160
Met Gln Leu Ser Leu Ala Glu Ser Glu Ala Ser Leu Gly Asn Thr Asn
705                 710                 715                 720

att cct gcc tca gac cac tac gtg ggg cca aat ggc ttt aaa agt ctg   2208
Ile Pro Ala Ser Asp His Tyr Val Gly Pro Asn Gly Phe Lys Ser Leu
                725                 730                 735

gct cag gag gcc aca aga tta gca gaa agc cac gtt gag tca gcc agt   2256
Ala Gln Glu Ala Thr Arg Leu Ala Glu Ser His Val Glu Ser Ala Ser
            740                 745                 750

aac atg gag caa ctg aca agg gaa act gag gac tat tcc aaa caa gcc   2304
Asn Met Glu Gln Leu Thr Arg Glu Thr Glu Asp Tyr Ser Lys Gln Ala
        755                 760                 765

ctc tca ctg gtg cgc aag gcc ctg cat gaa gga gtc gga agc gga agc   2352
Leu Ser Leu Val Arg Lys Ala Leu His Glu Gly Val Gly Ser Gly Ser
    770                 775                 780

ggt agc ccg gac ggt gct gtg gtg caa ggg ctt gtg gaa aaa ttg gag   2400
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Gly Ser Pro Asp Gly Ala Val Val Gln Gly Leu Val Glu Lys Leu Glu
785                 790                 795                 800

aaa acc aag tcc ctg gcc cag cag ttg aca agg gag gcc act caa gcg   2448
Lys Thr Lys Ser Leu Ala Gln Gln Leu Thr Arg Glu Ala Thr Gln Ala
                805                 810                 815

gaa att gaa gca gat agg tct tat cag cac agt ctc cgc ctc ctg gat   2496
Glu Ile Glu Ala Asp Arg Ser Tyr Gln His Ser Leu Arg Leu Leu Asp
            820                 825                 830

tca gtg tct ccg ctt cag gga gtc agt gat cag tcc ttt cag gtg gaa   2544
Ser Val Ser Pro Leu Gln Gly Val Ser Asp Gln Ser Phe Gln Val Glu
        835                 840                 845

gaa gca aag agg atc aaa caa aaa gcg gat tca ctc tca agc ctg gta   2592
Glu Ala Lys Arg Ile Lys Gln Lys Ala Asp Ser Leu Ser Ser Leu Val
    850                 855                 860

acc agg cat atg gat gag ttc aag cgt aca caa aag aat ctg gga aac   2640
Thr Arg His Met Asp Glu Phe Lys Arg Thr Gln Lys Asn Leu Gly Asn
865                 870                 875                 880

tgg aaa gaa gaa gca cag cag ctc tta cag aat gga aaa agt ggg aga   2688
Trp Lys Glu Glu Ala Gln Gln Leu Leu Gln Asn Gly Lys Ser Gly Arg
                885                 890                 895

gag aaa tca gat cag ctg ctt tcc cgt gcc aat ctt gct aaa agc aga   2736
Glu Lys Ser Asp Gln Leu Leu Ser Arg Ala Asn Leu Ala Lys Ser Arg
            900                 905                 910

gca caa gaa gca ctg agt atg ggc aat gcc act ttt tat gaa gtt gag   2784
Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr Phe Tyr Glu Val Glu
        915                 920                 925

agc atc ctt aaa aac ctc aga gag ttt gac ctg cag gtg gac aac aga   2832
Ser Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu Gln Val Asp Asn Arg
    930                 935                 940

aaa gca gaa gct gaa gaa gcc atg aag aga ctc tcc tac atc agc cag   2880
Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu Ser Tyr Ile Ser Gln
945                 950                 955                 960

aag gtt tca gat gcc agt gac aag acc cag caa gca gaa aga gcc ctg   2928
Lys Val Ser Asp Ala Ser Asp Lys Thr Gln Gln Ala Glu Arg Ala Leu
                965                 970                 975

ggg agc gct gct gct gat gca cag agg gca aag aat ggg gcc ggg gag   2976
Gly Ser Ala Ala Ala Asp Ala Gln Arg Ala Lys Asn Gly Ala Gly Glu
            980                 985                 990

gcc ctg gaa atc tcc agt gag att gaa cag gag att ggg agt ctg aac   3024
Ala Leu Glu Ile Ser Ser Glu Ile Glu Gln Glu Ile Gly Ser Leu Asn
        995                1000                1005

ttg gaa gcc aat gtg aca gca gat gga gcc ttg gcc atg gaa aag gga   3072
Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu Ala Met Glu Lys Gly
   1010                1015                1020

ctg gcc tct ctg aag agt gag atg agg gaa gtg gaa gga gag ctg gaa   3120
Leu Ala Ser Leu Lys Ser Glu Met Arg Glu Val Glu Gly Glu Leu Glu
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agg aag gag ctg gag ttt gac acg aat atg gat gca gta cag atg gtg   3168
Arg Lys Glu Leu Glu Phe Asp Thr Asn Met Asp Ala Val Gln Met Val
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att aca gaa gcc cag aag gtt gat acc aga gcc aag aac gct ggg gtt   3216
Ile Thr Glu Ala Gln Lys Val Asp Thr Arg Ala Lys Asn Ala Gly Val
            1060                1065                1070

aca atc caa gac aca ctc aac aca tta gac ggc ctc ctg cat ctg atg   3264
Thr Ile Gln Asp Thr Leu Asn Thr Leu Asp Gly Leu Leu His Leu Met
        1075                1080                1085

gac cag cct ctc agt gta gat gaa gag ggg ctg gtc tta ctg gag cag   3312
Asp Gln Pro Leu Ser Val Asp Glu Glu Gly Leu Val Leu Leu Glu Gln
    1090                1095                1100

aag ctt tcc cga gcc aag acc cag atc aac agc caa ctg cgg ccc atg   3360
Lys Leu Ser Arg Ala Lys Thr Gln Ile Asn Ser Gln Leu Arg Pro Met
1105                1110                1115                1120

atg tca gag ctg gaa gag agg gca cgt cag cag agg ggc cac ctc cat   3408
Met Ser Glu Leu Glu Glu Arg Ala Arg Gln Gln Arg Gly His Leu His
                1125                1130                1135

ttg ctg gag aca agc ata gat ggg att ctg gct gat gtg aag aac ttg   3456
Leu Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp Val Lys Asn Leu
            1140                1145                1150

gag aac att agg gac aac ctg ccc cca ggc tgc tac aat acc cag gct   3504
Glu Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys Tyr Asn Thr Gln Ala
        1155                1160                1165

ctt gag caa cag tgaagctgcc ataaatattt ctcaactgag gttcttggga       3556
Leu Glu Gln Gln
    1170

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Leu Asn Cys Asn Asp Asn Thr Asp Gly Ile His Cys Glu Lys Cys Lys
         35                  40                  45

Asn Gly Phe Tyr Arg His Arg Glu Arg Asp Arg Cys Leu Pro Cys Asn
     50                  55                  60

Cys Asn Ser Lys Gly Ser Leu Ser Ala Arg Cys Asp Asn Ser Gly Arg
 65                  70                  75                  80

Cys Ser Cys Lys Pro Gly Val Thr Gly Ala Arg Cys Asp Arg Cys Leu
                 85                  90                  95

Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys Thr Gln Asp Gln Arg
            100                 105                 110

Leu Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala Gly Ile Ala Gly Pro
        115                 120                 125

Cys Asp Ala Gly Arg Cys Val Cys Lys Pro Ala Val Thr Gly Glu Arg
    130                 135                 140
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Cys Asp Arg Cys Arg Ser Gly Tyr Tyr Asn Leu Asp Gly Gly Asn Pro
145                 150                 155                 160

Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His Ser Ala Ser Cys Arg
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Ser Ser Ala Glu Tyr Ser Val His Lys Ile Thr Ser Thr Phe His Gln
            180                 185                 190

Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn Gly Ser Pro Ala Lys
        195                 200                 205

Leu Gln Trp Ser Gln Arg His Gln Asp Val Phe Ser Ser Ala Gln Arg
    210                 215                 220

Leu Asp Pro Val Tyr Phe Val Ala Pro Ala Lys Phe Leu Gly Asn Gln
225                 230                 235                 240

Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp Tyr Arg Val Asp Arg
                245                 250                 255

Gly Gly Arg His Pro Ser Ala His Asp Val Ile Leu Glu Gly Ala Gly
            260                 265                 270

Leu Arg Ile Thr Ala Pro Leu Met Pro Leu Gly Lys Thr Leu Pro Cys
        275                 280                 285

Gly Leu Thr Lys Thr Tyr Thr Phe Arg Leu Asn Glu His Pro Ser Asn
    290                 295                 300

Asn Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr Arg Arg Leu Leu Arg
305                 310                 315                 320

Asn Leu Thr Ala Leu Arg Ile Arg Ala Thr Tyr Gly Glu Tyr Ser Thr
                325                 330                 335

Gly Tyr Ile Asp Asn Val Thr Leu Ile Ser Ala Arg Pro Val Ser Gly
            340                 345                 350

Ala Pro Ala Pro Trp Val Glu Gln Cys Ile Cys Pro Val Gly Tyr Lys
        355                 360                 365

Gly Gln Phe Cys Gln Asp Cys Ala Ser Gly Tyr Lys Arg Asp Ser Ala
    370                 375                 380

Arg Leu Gly Pro Phe Gly Thr Cys Ile Pro Cys Asn Cys Gln Gly Gly
385                 390                 395                 400

Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr Ser Gly Asp Glu Asn
                405                 410                 415

Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly Phe Tyr Asn Asp Pro
            420                 425                 430

His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys His Asn Gly Phe Ser
        435                 440                 445

Cys Ser Val Ile Pro Glu Thr Glu Glu Val Val Cys Asn Asn Cys Pro
    450                 455                 460

Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys Ala Asp Gly Tyr Phe
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465                 470                 475                 480

Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg Pro Cys Gln Pro Cys
                485                 490                 495

Gln Cys Asn Ser Asn Val Asp Pro Ser Ala Ser Gly Asn Cys Asp Arg
            500                 505                 510

Leu Thr Gly Arg Cys Leu Lys Cys Ile His Asn Thr Ala Gly Ile Tyr
        515                 520                 525

Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp Pro Leu Ala Pro Asn
    530                 535                 540

Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Asn Pro Met Gly Ser Glu
545                 550                 555                 560

Pro Val Gly Cys Arg Ser Asp Gly Thr Cys Val Cys Lys Pro Gly Phe
                565                 570                 575

Gly Gly Pro Asn Cys Glu His Gly Ala Phe Ser Cys Pro Ala Cys Tyr
            580                 585                 590

Asn Gln Val Lys Ile Gln Met Asp Gln Phe Met Gln Gln Leu Gln Arg
        595                 600                 605

Met Glu Ala Leu Ile Ser Lys Ala Gln Gly Gly Asp Gly Val Val Pro
    610                 615                 620

Asp Thr Glu Leu Glu Gly Arg Met Gln Gln Ala Glu Gln Ala Leu Gln
625                 630                 635                 640

Asp Ile Leu Arg Asp Ala Gln Ile Ser Glu Gly Ala Ser Arg Ser Leu
                645                 650                 655

Gly Leu Gln Leu Ala Lys Val Arg Ser Gln Glu Asn Ser Tyr Gln Ser
            660                 665                 670

Arg Leu Asp Asp Leu Lys Met Thr Val Glu Arg Val Arg Ala Leu Gly
        675                 680                 685

Ser Gln Tyr Gln Asn Arg Val Arg Asp Thr His Arg Leu Ile Thr Gln
    690                 695                 700

Met Gln Leu Ser Leu Ala Glu Ser Glu Ala Ser Leu Gly Asn Thr Asn
705                 710                 715                 720

Ile Pro Ala Ser Asp His Tyr Val Gly Pro Asn Gly Phe Lys Ser Leu
                725                 730                 735

Ala Gln Glu Ala Thr Arg Leu Ala Glu Ser His Val Glu Ser Ala Ser
            740                 745                 750

Asn Met Glu Gln Leu Thr Arg Glu Thr Glu Asp Tyr Ser Lys Gln Ala
        755                 760                 765

Leu Ser Leu Val Arg Lys Ala Leu His Glu Gly Val Gly Ser Gly Ser
    770                 775                 780

Gly Ser Pro Asp Gly Ala Val Val Gln Gly Leu Val Glu Lys Leu Glu
785                 790                 795                 800
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Lys Thr Lys Ser Leu Ala Gln Gln Leu Thr Arg Glu Ala Thr Gln Ala
                805                 810                 815

Glu Ile Glu Ala Asp Arg Ser Tyr Gln His Ser Leu Arg Leu Leu Asp
            820                 825                 830

Ser Val Ser Pro Leu Gln Gly Val Ser Asp Gln Ser Phe Gln Val Glu
        835                 840                 845

Glu Ala Lys Arg Ile Lys Gln Lys Ala Asp Ser Leu Ser Ser Leu Val
    850                 855                 860

Thr Arg His Met Asp Glu Phe Lys Arg Thr Gln Lys Asn Leu Gly Asn
865                 870                 875                 880

Trp Lys Glu Glu Ala Gln Gln Leu Leu Gln Asn Gly Lys Ser Gly Arg
                885                 890                 895

Glu Lys Ser Asp Gln Leu Leu Ser Arg Ala Asn Leu Ala Lys Ser Arg
            900                 905                 910

Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr Phe Tyr Glu Val Glu
        915                 920                 925

Ser Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu Gln Val Asp Asn Arg
    930                 935                 940

Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu Ser Tyr Ile Ser Gln
945                 950                 955                 960

Lys Val Ser Asp Ala Ser Asp Lys Thr Gln Gln Ala Glu Arg Ala Leu
                965                 970                 975

Gly Ser Ala Ala Ala Asp Ala Gln Arg Ala Lys Asn Gly Ala Gly Glu
            980                 985                 990

Ala Leu Glu Ile Ser Ser Glu Ile Glu Gln Glu Ile Gly Ser Leu Asn
        995                1000                1005

Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu Ala Met Glu Lys Gly
   1010                1015                1020

Leu Ala Ser Leu Lys Ser Glu Met Arg Glu Val Glu Gly Glu Leu Glu
1025                1030                1035                1040

Arg Lys Glu Leu Glu Phe Asp Thr Asn Met Asp Ala Val Gln Met Val
                1045                1050                1055

Ile Thr Glu Ala Gln Lys Val Asp Thr Arg Ala Lys Asn Ala Gly Val
           1060                1065                1070

Thr Ile Gln Asp Thr Leu Asn Thr Leu Asp Gly Leu Leu His Leu Met
       1075                1080                1085

Asp Gln Pro Leu Ser Val Asp Glu Glu Gly Leu Val Leu Leu Glu Gln
   1090                1095                1100

Lys Leu Ser Arg Ala Lys Thr Gln Ile Asn Ser Gln Leu Arg Pro Met
1105                1110                1115                1120
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Met Ser Glu Leu Glu Glu Arg Ala Arg Gln Gln Arg Gly His Leu His
1125 1130 1135

Leu Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp Val Lys Asn Leu
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Glu Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys Tyr Asn Thr Gln Ala
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Leu Glu Gln Gln
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Met Pro Ala Leu Trp Leu
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ggc tgc tgc ctc tgc ttc tcg ctc ctc ctg ccc gca gcc cgg gcc acc 103
Gly Cys Cys Leu Cys Phe Ser Leu Leu Leu Pro Ala Ala Arg Ala Thr
10 15 20

tcc agg agg gaa gtc tgt gat tgc aat ggg aag tcc agg cag tgt atc 151
Ser Arg Arg Glu Val Cys Asp Cys Asn Gly Lys Ser Arg Gln Cys Ile
25 30 35

ttt gat cgg gaa ctt cac aga caa act ggt aat gga ttc cgc tgc ctc 199
Phe Asp Arg Glu Leu His Arg Gln Thr Gly Asn Gly Phe Arg Cys Leu
40 45 50

aac tgc aat gac aac act gat ggc att cac tgc gag aag tgc aag aat 247
Asn Cys Asn Asp Asn Thr Asp Gly Ile His Cys Glu Lys Cys Lys Asn
55 60 65 70

ggc ttt tac cgg cac aga gaa agg gac cgc tgt ttg ccc tgc aat tgt 295
Gly Phe Tyr Arg His Arg Glu Arg Asp Arg Cys Leu Pro Cys Asn Cys
75 80 85

aac tcc aaa ggt tct ctt agt gct cga tgt gac aac tct gga cgg tgc 343
Asn Ser Lys Gly Ser Leu Ser Ala Arg Cys Asp Asn Ser Gly Arg Cys
90 95 100

agc tgt aaa cca ggt gtg aca gga gcc aga tgc gac cga tgt ctg cca 391
Ser Cys Lys Pro Gly Val Thr Gly Ala Arg Cys Asp Arg Cys Leu Pro
105 110 115

ggc ttc cac atg ctc acg gat gcg ggg tgc acc caa gac cag aga ctg 439
Gly Phe His Met Leu Thr Asp Ala Gly Cys Thr Gln Asp Gln Arg Leu

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    120                 125                 130

cta gac tcc aag tgt gac tgt gac cca gct ggc atc gca ggg ccc tgt   487
Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala Gly Ile Ala Gly Pro Cys
135                 140                 145                 150

gac gcg ggc cgc tgt gtc tgc aag cca gct gtt act gga gaa cgc tgt   535
Asp Ala Gly Arg Cys Val Cys Lys Pro Ala Val Thr Gly Glu Arg Cys
                155                 160                 165

gat ggg tgt cga tca ggt tac tat aat ctg gat ggg ggg aac cct gag   583
Asp Gly Cys Arg Ser Gly Tyr Tyr Asn Leu Asp Gly Gly Asn Pro Glu
            170                 175                 180

ggc tgt acc cag tgt ttc tgc tat ggg cat tca gcc agc tgc cgc agc   631
Gly Cys Thr Gln Cys Phe Cys Tyr Gly His Ser Ala Ser Cys Arg Ser
        185                 190                 195

tct gca gaa tac agt gtc cat aag atc acc tct acc ttt cat caa gat   679
Ser Ala Glu Tyr Ser Val His Lys Ile Thr Ser Thr Phe His Gln Asp
    200                 205                 210

gtt gat ggc tgg aag gct gtc caa cga aat ggg tct cct gca aag ctc   727
Val Asp Gly Trp Lys Ala Val Gln Arg Asn Gly Ser Pro Ala Lys Leu
215                 220                 225                 230

caa tgg tca cag cgc cat caa gat gtg ttt agc tca gcc caa cga cta   775
Gln Trp Ser Gln Arg His Gln Asp Val Phe Ser Ser Ala Gln Arg Leu
                235                 240                 245

gac cct gtc tat ttt gtg gct cct gcc aaa ttt ctt ggg aat caa cag   823
Asp Pro Val Tyr Phe Val Ala Pro Ala Lys Phe Leu Gly Asn Gln Gln
            250                 255                 260

gtg agc tat ggg caa agc ctg tcc ttt gac tac cgt gtg gac aga gga   871
Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp Tyr Arg Val Asp Arg Gly
        265                 270                 275

ggc aga cac cca tct gcc cat gat gtg att ctg gaa ggt gct ggt cta   919
Gly Arg His Pro Ser Ala His Asp Val Ile Leu Glu Gly Ala Gly Leu
    280                 285                 290

cgg atc aca gct ccc ttg atg cca ctt ggc aag aca ctg cct tgt ggg   967
Arg Ile Thr Ala Pro Leu Met Pro Leu Gly Lys Thr Leu Pro Cys Gly
295                 300                 305                 310

ctc acc aag act tac aca ttc agg tta aat gag cat cca agc aat aat  1015
Leu Thr Lys Thr Tyr Thr Phe Arg Leu Asn Glu His Pro Ser Asn Asn
                315                 320                 325

tgg agc ccc cag ctg agt tac ttt gag tat cga agg tta ctg cgg aat  1063
Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr Arg Arg Leu Leu Arg Asn
            330                 335                 340

ctc aca gcc ctc cgc atc cga gct aca tat gga gaa tac agt act ggg  1111
Leu Thr Ala Leu Arg Ile Arg Ala Thr Tyr Gly Glu Tyr Ser Thr Gly
        345                 350                 355

tac att gac aat gtg acc ctg att tca gcc cgc cct gtc tct gga gcc  1159
Tyr Ile Asp Asn Val Thr Leu Ile Ser Ala Arg Pro Val Ser Gly Ala
    360                 365                 370
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cca gca ccc tgg gtt gaa cag tgt ata tgt cct gtt ggg tac aag ggg   1207
Pro Ala Pro Trp Val Glu Gln Cys Ile Cys Pro Val Gly Tyr Lys Gly
375                 380                 385                 390

caa ttc tgc cag gat tgt gct tct ggc tac aag aga gat tca gcg aga   1255
Gln Phe Cys Gln Asp Cys Ala Ser Gly Tyr Lys Arg Asp Ser Ala Arg
                395                 400                 405

ctg ggg cct ttt ggc acc tgt att cct tgt aac tgt caa ggg gga ggg   1303
Leu Gly Pro Phe Gly Thr Cys Ile Pro Cys Asn Cys Gln Gly Gly Gly
            410                 415                 420

gcc tgt gat cca gac aca gga gat tgt tat tca ggg gat gag aat cct   1351
Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr Ser Gly Asp Glu Asn Pro
        425                 430                 435

gac att gag tgt gct gac tgc cca att ggt ttc tac aac gat ccg cac   1399
Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly Phe Tyr Asn Asp Pro His
    440                 445                 450

gac ccc cgc agc tgc aag cca tgt ccc tgt cat aac ggg ttc agc tgc   1447
Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys His Asn Gly Phe Ser Cys
455                 460                 465                 470

tca gtg atg ccg gag acg gag gag gtg gtg tgc aat aac tgc cct ccc   1495
Ser Val Met Pro Glu Thr Glu Glu Val Val Cys Asn Asn Cys Pro Pro
                475                 480                 485

ggg gtc acc ggt gcc cgc tgt gag ctc tgt gct gat ggc tac ttt ggg   1543
Gly Val Thr Gly Ala Arg Cys Glu Leu Cys Ala Asp Gly Tyr Phe Gly
            490                 495                 500

gac ccc ttt ggt gaa cat ggc cca gtg agg cct tgt cag ccc tgt caa   1591
Asp Pro Phe Gly Glu His Gly Pro Val Arg Pro Cys Gln Pro Cys Gln
        505                 510                 515

tgc aac aac aat gtg gac ccc agt gcc tct ggg aat tgt gac cgg ctg   1639
Cys Asn Asn Asn Val Asp Pro Ser Ala Ser Gly Asn Cys Asp Arg Leu
    520                 525                 530

aca ggc agg tgt ttg aag tgt atc cac aac aca gcc ggc atc tac tgc   1687
Thr Gly Arg Cys Leu Lys Cys Ile His Asn Thr Ala Gly Ile Tyr Cys
535                 540                 545                 550

gac cag tgc aaa gca ggc tac ttc ggg gac cca ttg gct ccc aac cca   1735
Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp Pro Leu Ala Pro Asn Pro
                555                 560                 565

gca gac aag tgt cga gct tgc aac tgt aac ccc atg ggc tca gag cct   1783
Ala Asp Lys Cys Arg Ala Cys Asn Cys Asn Pro Met Gly Ser Glu Pro
            570                 575                 580

gta gga tgt cga agt gat ggc acc tgt gtt tgc aag cca gga ttt ggt   1831
Val Gly Cys Arg Ser Asp Gly Thr Cys Val Cys Lys Pro Gly Phe Gly
        585                 590                 595

ggc ccc aac tgt gag cat gga gca ttc agc tgt cca gct tgc tat aat   1879
Gly Pro Asn Cys Glu His Gly Ala Phe Ser Cys Pro Ala Cys Tyr Asn
    600                 605                 610
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caa gtg aag att cag atg gat cag ttt atg cag cag ctt cag aga atg   1927
Gln Val Lys Ile Gln Met Asp Gln Phe Met Gln Gln Leu Gln Arg Met
615                 620                 625                 630

gag gcc ctg att tca aag gct cag ggt ggt gat gga gta gta cct gat   1975
Glu Ala Leu Ile Ser Lys Ala Gln Gly Gly Asp Gly Val Val Pro Asp
                635                 640                 645

aca gag ctg gaa ggc agg atg cag cag gct gag cag gcc ctt cag gac   2023
Thr Glu Leu Glu Gly Arg Met Gln Gln Ala Glu Gln Ala Leu Gln Asp
            650                 655                 660

att ctg aga gat gcc cag att tca gaa ggt gct agc aga tcc ctt ggt   2071
Ile Leu Arg Asp Ala Gln Ile Ser Glu Gly Ala Ser Arg Ser Leu Gly
        665                 670                 675

ctc cag ttg gcc aag gtg agg agc caa gag aac agc tac cag agc cgc   2119
Leu Gln Leu Ala Lys Val Arg Ser Gln Glu Asn Ser Tyr Gln Ser Arg
    680                 685                 690

ctg gat gac ctc aag atg act gtg gaa aga gtt cgg gct ctg gga agt   2167
Leu Asp Asp Leu Lys Met Thr Val Glu Arg Val Arg Ala Leu Gly Ser
695                 700                 705                 710

cag tac cag aac cga gtt cgg gat act cac agg ctc atc act cag atg   2215
Gln Tyr Gln Asn Arg Val Arg Asp Thr His Arg Leu Ile Thr Gln Met
                715                 720                 725

cag ctg agc ctg gca gaa agt gaa gct tcc ttg gga aac act aac att   2263
Gln Leu Ser Leu Ala Glu Ser Glu Ala Ser Leu Gly Asn Thr Asn Ile
            730                 735                 740

cct gcc tca gac cac tac gtg ggg cca aat ggc ttt aaa agt ctg gct   2311
Pro Ala Ser Asp His Tyr Val Gly Pro Asn Gly Phe Lys Ser Leu Ala
        745                 750                 755

cag gag gcc aca aga tta gca gaa agc cac gtt gag tca gcc agt aac   2359
Gln Glu Ala Thr Arg Leu Ala Glu Ser His Val Glu Ser Ala Ser Asn
    760                 765                 770

atg gag caa ctg aca agg gaa act gag gac tat tcc aaa caa gcc ctc   2407
Met Glu Gln Leu Thr Arg Glu Thr Glu Asp Tyr Ser Lys Gln Ala Leu
775                 780                 785                 790

tca ctg gtg cgc aag gcc ctg cat gaa gga gtc gga agc gga agc ggt   2455
Ser Leu Val Arg Lys Ala Leu His Glu Gly Val Gly Ser Gly Ser Gly
                795                 800                 805

agc ccg gac ggt gct gtg gtg caa ggg ctt gtg gaa aaa ttg gag aaa   2503
Ser Pro Asp Gly Ala Val Val Gln Gly Leu Val Glu Lys Leu Glu Lys
            810                 815                 820

acc aag tcc ctg gcc cag cag ttg aca agg gag gcc act caa gcg gaa   2551
Thr Lys Ser Leu Ala Gln Gln Leu Thr Arg Glu Ala Thr Gln Ala Glu
        825                 830                 835

att gaa gca gat agg tct tat cag cac agt ctc cgc ctc ctg gat tca   2599
Ile Glu Ala Asp Arg Ser Tyr Gln His Ser Leu Arg Leu Leu Asp Ser
    840                 845                 850

gtg tct ccg ctt cag gga gtc agt gat cag tcc ttt cag gtg gaa gaa   2647
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Val Ser Pro Leu Gln Gly Val Ser Asp Gln Ser Phe Gln Val Glu Glu
855                 860                 865                 870

gca aag agg atc aaa caa aaa gcg gat tca ctc tca agc ctg gta acc   2695
Ala Lys Arg Ile Lys Gln Lys Ala Asp Ser Leu Ser Ser Leu Val Thr
                875                 880                 885

agg cat atg gat gag ttc aag cgt aca caa aag aat ctg gga aac tgg   2743
Arg His Met Asp Glu Phe Lys Arg Thr Gln Lys Asn Leu Gly Asn Trp
            890                 895                 900

aaa gaa gaa gca cag cag ctc tta cag aat gga aaa agt ggg aga gag   2791
Lys Glu Glu Ala Gln Gln Leu Leu Gln Asn Gly Lys Ser Gly Arg Glu
        905                 910                 915

aaa tca gat cag ctg ctt tcc cgt gcc aat ctt gct aaa agc aga gca   2839
Lys Ser Asp Gln Leu Leu Ser Arg Ala Asn Leu Ala Lys Ser Arg Ala
    920                 925                 930

caa gaa gca ctg agt atg ggc aat gcc act ttt tat gaa gtt gag agc   2887
Gln Glu Ala Leu Ser Met Gly Asn Ala Thr Phe Tyr Glu Val Glu Ser
935                 940                 945                 950

atc ctt aaa aac ctc aga gag ttt gac ctg cag gtg gac aac aga aaa   2935
Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu Gln Val Asp Asn Arg Lys
                955                 960                 965

gca gaa gct gaa gaa gcc atg aag aga ctc tcc tac atc agc cag aag   2983
Ala Glu Ala Glu Glu Ala Met Lys Arg Leu Ser Tyr Ile Ser Gln Lys
            970                 975                 980

gtt tca gat gcc agt gac aag acc cag caa gca gaa aga gcc ctg ggg   3031
Val Ser Asp Ala Ser Asp Lys Thr Gln Gln Ala Glu Arg Ala Leu Gly
        985                 990                 995

agc gct gct gct gat gca cag agg gca aag aat ggg gcc ggg gag gcc   3079
Ser Ala Ala Ala Asp Ala Gln Arg Ala Lys Asn Gly Ala Gly Glu Ala
   1000                1005                1010

ctg gaa atc tcc agt gag att gaa cag gag att ggg agt ctg aac ttg   3127
Leu Glu Ile Ser Ser Glu Ile Glu Gln Glu Ile Gly Ser Leu Asn Leu
1015                1020                1025                1030

gaa gcc aat gtg aca gca gat gga gcc ttg gcc atg gaa aag gga ctg   3175
Glu Ala Asn Val Thr Ala Asp Gly Ala Leu Ala Met Glu Lys Gly Leu
                1035                1040                1045

gcc tct ctg aag agt gag atg agg gaa gtg gaa gga gag ctg gaa agg   3223
Ala Ser Leu Lys Ser Glu Met Arg Glu Val Glu Gly Glu Leu Glu Arg
            1050                1055                1060

aag gag ctg gag ttt gac acg aat atg gat gca gta cag atg gtg att   3271
Lys Glu Leu Glu Phe Asp Thr Asn Met Asp Ala Val Gln Met Val Ile
        1065                1070                1075

aca gaa gcc cag aag gtt gat acc aga gcc aag aac gct ggg gtt aca   3319
Thr Glu Ala Gln Lys Val Asp Thr Arg Ala Lys Asn Ala Gly Val Thr
   1080                1085                1090

atc caa gac aca ctc aac aca tta gac ggc ctc ctg cat ctg atg gac   3367
Ile Gln Asp Thr Leu Asn Thr Leu Asp Gly Leu Leu His Leu Met Asp
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cag cct ctc agt gta gat gaa gag ggg ctg gtc tta ctg gag cag aag   3415
Gln Pro Leu Ser Val Asp Glu Glu Gly Leu Val Leu Leu Glu Gln Lys
                1115                1120                1125

ctt tcc cga gcc aag acc cag atc aac agc caa ctg cgg ccc atg atg   3463
Leu Ser Arg Ala Lys Thr Gln Ile Asn Ser Gln Leu Arg Pro Met Met
            1130                1135                1140

tca gag ctg gaa gag agg gca cgt cag cag agg ggc cac ctc cat ttg   3511
Ser Glu Leu Glu Glu Arg Ala Arg Gln Gln Arg Gly His Leu His Leu
        1145                1150                1155

ctg gag aca agc ata gat ggg att ctg gct gat gtg aag aac ttg gag   3559
Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp Val Lys Asn Leu Glu
    1160                1165                1170

aac att agg gac aac ctg ccc cca ggc tgc tac aat acc cag gct ctt   3607
Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys Tyr Asn Thr Gln Ala Leu
1175                1180                1185                1190

gag caa cag tgaagctgcc ataaatattt ctcaactgag gttcttggga           3656
Glu Gln Gln

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atgt                                                              3720


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            20                  25                  30

Lys Ser Arg Gln Cys Ile Phe Asp Arg Glu Leu His Arg Gln Thr Gly
        35                  40                  45

Asn Gly Phe Arg Cys Leu Asn Cys Asn Asp Asn Thr Asp Gly Ile His
    50                  55                  60

Cys Glu Lys Cys Lys Asn Gly Phe Tyr Arg His Arg Glu Arg Asp Arg
65                  70                  75                  80

Cys Leu Pro Cys Asn Cys Asn Ser Lys Gly Ser Leu Ser Ala Arg Cys
                85                  90                  95

Asp Asn Ser Gly Arg Cys Ser Cys Lys Pro Gly Val Thr Gly Ala Arg
            100                 105                 110

Cys Asp Arg Cys Leu Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys
        115                 120                 125

Thr Gln Asp Gln Arg Leu Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala
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    130                 135                 140

Gly Ile Ala Gly Pro Cys Asp Ala Gly Arg Cys Val Cys Lys Pro Ala
145                 150                 155                 160

Val Thr Gly Glu Arg Cys Asp Gly Cys Arg Ser Gly Tyr Tyr Asn Leu
                165                 170                 175

Asp Gly Gly Asn Pro Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His
            180                 185                 190

Ser Ala Ser Cys Arg Ser Ser Ala Glu Tyr Ser Val His Lys Ile Thr
        195                 200                 205

Ser Thr Phe His Gln Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn
    210                 215                 220

Gly Ser Pro Ala Lys Leu Gln Trp Ser Gln Arg His Gln Asp Val Phe
225                 230                 235                 240

Ser Ser Ala Gln Arg Leu Asp Pro Val Tyr Phe Val Ala Pro Ala Lys
                245                 250                 255

Phe Leu Gly Asn Gln Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp
            260                 265                 270

Tyr Arg Val Asp Arg Gly Gly Arg His Pro Ser Ala His Asp Val Ile
        275                 280                 285

Leu Glu Gly Ala Gly Leu Arg Ile Thr Ala Pro Leu Met Pro Leu Gly
    290                 295                 300

Lys Thr Leu Pro Cys Gly Leu Thr Lys Thr Tyr Thr Phe Arg Leu Asn
305                 310                 315                 320

Glu His Pro Ser Asn Asn Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr
                325                 330                 335

Arg Arg Leu Leu Arg Asn Leu Thr Ala Leu Arg Ile Arg Ala Thr Tyr
            340                 345                 350

Gly Glu Tyr Ser Thr Gly Tyr Ile Asp Asn Val Thr Leu Ile Ser Ala
        355                 360                 365

Arg Pro Val Ser Gly Ala Pro Ala Pro Trp Val Glu Gln Cys Ile Cys
    370                 375                 380

Pro Val Gly Tyr Lys Gly Gln Phe Cys Gln Asp Cys Ala Ser Gly Tyr
385                 390                 395                 400

Lys Arg Asp Ser Ala Arg Leu Gly Pro Phe Gly Thr Cys Ile Pro Cys
                405                 410                 415

Asn Cys Gln Gly Gly Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr
            420                 425                 430

Ser Gly Asp Glu Asn Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly
        435                 440                 445

Phe Tyr Asn Asp Pro His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys
    450                 455                 460
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His Asn Gly Phe Ser Cys Ser Val Met Pro Glu Thr Glu Glu Val Val
465                 470                 475                 480

Cys Asn Asn Cys Pro Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys
                485                 490                 495

Ala Asp Gly Tyr Phe Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg
            500                 505                 510

Pro Cys Gln Pro Cys Gln Cys Asn Asn Asn Val Asp Pro Ser Ala Ser
        515                 520                 525

Gly Asn Cys Asp Arg Leu Thr Gly Arg Cys Leu Lys Cys Ile His Asn
    530                 535                 540

Thr Ala Gly Ile Tyr Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp
545                 550                 555                 560

Pro Leu Ala Pro Asn Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Asn
                565                 570                 575

Pro Met Gly Ser Glu Pro Val Gly Cys Arg Ser Asp Gly Thr Cys Val
            580                 585                 590

Cys Lys Pro Gly Phe Gly Gly Pro Asn Cys Glu His Gly Ala Phe Ser
        595                 600                 605

Cys Pro Ala Cys Tyr Asn Gln Val Lys Ile Gln Met Asp Gln Phe Met
    610                 615                 620

Gln Gln Leu Gln Arg Met Glu Ala Leu Ile Ser Lys Ala Gln Gly Gly
625                 630                 635                 640

Asp Gly Val Val Pro Asp Thr Glu Leu Glu Gly Arg Met Gln Gln Ala
                645                 650                 655

Glu Gln Ala Leu Gln Asp Ile Leu Arg Asp Ala Gln Ile Ser Glu Gly
            660                 665                 670

Ala Ser Arg Ser Leu Gly Leu Gln Leu Ala Lys Val Arg Ser Gln Glu
        675                 680                 685

Asn Ser Tyr Gln Ser Arg Leu Asp Asp Leu Lys Met Thr Val Glu Arg
    690                 695                 700

Val Arg Ala Leu Gly Ser Gln Tyr Gln Asn Arg Val Arg Asp Thr His
705                 710                 715                 720

Arg Leu Ile Thr Gln Met Gln Leu Ser Leu Ala Glu Ser Glu Ala Ser
                725                 730                 735

Leu Gly Asn Thr Asn Ile Pro Ala Ser Asp His Tyr Val Gly Pro Asn
            740                 745                 750

Gly Phe Lys Ser Leu Ala Gln Glu Ala Thr Arg Leu Ala Glu Ser His
        755                 760                 765

Val Glu Ser Ala Ser Asn Met Glu Gln Leu Thr Arg Glu Thr Glu Asp
    770                 775                 780
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Tyr Ser Lys Gln Ala Leu Ser Leu Val Arg Lys Ala Leu His Glu Gly
785                 790                 795                 800

Val Gly Ser Gly Ser Gly Ser Pro Asp Gly Ala Val Val Gln Gly Leu
                805                 810                 815

Val Glu Lys Leu Gln Lys Thr Lys Ser Leu Ala Gln Gln Leu Thr Arg
            820                 825                 830

Glu Ala Thr Gln Ala Glu Ile Glu Ala Asp Arg Ser Tyr Gln His Ser
        835                 840                 845

Leu Arg Leu Leu Asp Ser Val Ser Pro Leu Gln Gly Val Ser Asp Gln
    850                 855                 860

Ser Phe Gln Val Glu Glu Ala Lys Arg Ile Lys Gln Lys Ala Asp Ser
865                 870                 875                 880

Leu Ser Ser Leu Val Thr Arg His Met Asp Glu Phe Lys Arg Thr Gln
                885                 890                 895

Lys Asn Leu Gly Asn Trp Lys Glu Glu Ala Gln Gln Leu Leu Gln Asn
            900                 905                 910

Gly Lys Ser Gly Arg Glu Lys Ser Asp Gln Leu Leu Ser Arg Ala Asn
        915                 920                 925

Leu Ala Lys Ser Arg Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr
    930                 935                 940

Phe Tyr Glu Val Glu Ser Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu
945                 950                 955                 960

Gln Val Asp Asn Arg Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu
                965                 970                 975

Ser Tyr Ile Ser Gln Lys Val Ser Asp Ala Ser Asp Lys Thr Gln Gln
            980                 985                 990

Ala Glu Arg Ala Leu Gly Ser Ala Ala Ala Asp Ala Gln Arg Ala Lys
        995                1000                1005

Asn Gly Ala Gly Glu Ala Leu Glu Ile Ser Ser Glu Ile Glu Gln Glu
   1010                1015                1020

Ile Gly Ser Leu Asn Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu
025                1030                1035                1040

Ala Met Glu Lys Gly Leu Ala Ser Leu Lys Ser Glu Met Arg Glu Val
               1045                1050                1055

Glu Gly Glu Leu Glu Arg Lys Glu Leu Glu Phe Asp Thr Asn Met Asp
           1060                1065                1070

Ala Val Gln Met Val Ile Thr Glu Ala Gln Lys Val Asp Thr Arg Ala
       1075                1080                1085

Lys Asn Ala Gly Val Thr Ile Gln Asp Thr Leu Asn Thr Leu Asp Gly
   1090                1095                1100

L u Leu His Leu Met Asp Gln Pro Leu Ser Val Asp Glu Glu Gly Leu
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105 1110 1115 1120

Val Leu Leu Glu Gln Lys Leu Ser Arg Ala Lys Thr Gln Ile Asn Ser
1125 1130 1135

Gln Leu Arg Pro Met Met Ser Glu Leu Glu Glu Arg Ala Arg Gln Gln
1140 1145 1150

Arg Gly His Leu His Leu Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala
1155 1160 1165

Asp Val Lys Asn Leu Glu Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys
1170 1175 1180

Tyr Asn Thr Gln Ala Leu Glu Gln Gln
185 1190

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<220>
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Thr Ser Arg Arg Glu Val Cys Asp Cys Asn Gly Lys Ser Arg Gln Cys
1 5 10 15

atc ttt gat cgg gaa ctt cac aga caa act ggt aat gga ttc cgc tgc 96
Ile Phe Asp Arg Glu Leu His Arg Gln Thr Gly Asn Gly Phe Arg Cys
20 25 30

ctc aac tgc aat gac aac act gat ggc att cac tgc gag aag tgc aag 144
Leu Asn Cys Asn Asp Asn Thr Asp Gly Ile His Cys Glu Lys Cys Lys
35 40 45

aat ggc ttt tac cgg cac aga gaa agg gac cgc tgt ttg ccc tgc aat 192
Asn Gly Phe Tyr Arg His Arg Glu Arg Asp Arg Cys Leu Pro Cys Asn
50 55 60

tgt aac tcc aaa ggt tct ctt agt gct cga tgt gac aac tct gga cgg 240
Cys Asn Ser Lys Gly Ser Leu Ser Ala Arg Cys Asp Asn Ser Gly Arg
65 70 75 80

tgc agc tgt aaa cca ggt gtg aca gga gcc aga tgc gac cga tgt ctg 288
Cys Ser Cys Lys Pro Gly Val Thr Gly Ala Arg Cys Asp Arg Cys Leu
85 90 95

cca ggc ttc cac atg ctc acg gat gcg ggg tgc acc caa gac cag aga 336
Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys Thr Gln Asp Gln Arg
100 105 110

ctg cta gac tcc aag tgt gac tgt gac cca gct ggc atc gca ggg ccc 384
Leu Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala Gly Ile Ala Gly Pro
115 120 125

tgt gac gcg ggc cgc tgt gtc tgc aag cca gct gtt act gga gaa cgc 432

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Cys Asp Ala Gly Arg Cys Val Cys Lys Pro Ala Val Thr Gly Glu Arg
    130                 135                 140

tgt gat ggg tgt cga tca ggt tac tat aat ctg gat ggg ggg aac cct   480
Cys Asp Gly Cys Arg Ser Gly Tyr Tyr Asn Leu Asp Gly Gly Asn Pro
145                 150                 155                 160

gag ggc tgt acc cag tgt ttc tgc tat ggg cat tca gcc agc tgc cgc   528
Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His Ser Ala Ser Cys Arg
                165                 170                 175

agc tct gca gaa tac agt gtc cat aag atc acc tct acc ttt cat caa   576
Ser Ser Ala Glu Tyr Ser Val His Lys Ile Thr Ser Thr Phe His Gln
            180                 185                 190

gat gtt gat ggc tgg aag gct gtc caa cga aat ggg tct cct gca aag   624
Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn Gly Ser Pro Ala Lys
        195                 200                 205

ctc caa tgg tca cag cgc cat caa gat gtg ttt agc tca gcc caa cga   672
Leu Gln Trp Ser Gln Arg His Gln Asp Val Phe Ser Ser Ala Gln Arg
    210                 215                 220

cta gac cct gtc tat ttt gtg gct cct gcc aaa ttt ctt ggg aat caa   720
Leu Asp Pro Val Tyr Phe Val Ala Pro Ala Lys Phe Leu Gly Asn Gln
225                 230                 235                 240

cag gtg agc tat ggg caa agc ctg tcc ttt gac tac cgt gtg gac aga   768
Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp Tyr Arg Val Asp Arg
                245                 250                 255

gga ggc aga cac cca tct gcc cat gat gtg att ctg gaa ggt gct ggt   816
Gly Gly Arg His Pro Ser Ala His Asp Val Ile Leu Glu Gly Ala Gly
            260                 265                 270

cta cgg atc aca gct ccc ttg atg cca ctt ggc aag aca ctg cct tgt   864
Leu Arg Ile Thr Ala Pro Leu Met Pro Leu Gly Lys Thr Leu Pro Cys
        275                 280                 285

ggg ctc acc aag act tac aca ttc agg tta aat gag cat cca agc aat   912
Gly Leu Thr Lys Thr Tyr Thr Phe Arg Leu Asn Glu His Pro Ser Asn
    290                 295                 300

aat tgg agc ccc cag ctg agt tac ttt gag tat cga agg tta ctg cgg   960
Asn Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr Arg Arg Leu Leu Arg
305                 310                 315                 320

aat ctc aca gcc ctc cgc atc cga gct aca tat gga gaa tac agt act   1008
Asn Leu Thr Ala Leu Arg Ile Arg Ala Thr Tyr Gly Glu Tyr Ser Thr
                325                 330                 335

ggg tac att gac aat gtg acc ctg att tca gcc cgc cct gtc tct gga   1056
Gly Tyr Ile Asp Asn Val Thr Leu Ile Ser Ala Arg Pro Val Ser Gly
            340                 345                 350

gcc cca gca ccc tgg gtt gaa cag tgt ata tgt cct gtt ggg tac aag   1104
Ala Pro Ala Pro Trp Val Glu Gln Cys Ile Cys Pro Val Gly Tyr Lys
        355                 360                 365

ggg caa ttc tgc cag gat tgt gct tct ggc tac aag aga gat tca gcg   1152
Gly Gln Phe Cys Gln Asp Cys Ala Ser Gly Tyr Lys Arg Asp Ser Ala
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    370                 375                 380

aga ctg ggg cct ttt ggc acc tgt att cct tgt aac tgt caa ggg gga   1200
Arg Leu Gly Pro Phe Gly Thr Cys Ile Pro Cys Asn Cys Gln Gly Gly
385                 390                 395                 400

ggg gcc tgt gat cca gac aca gga gat tgt tat tca ggg gat gag aat   1248
Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr Ser Gly Asp Glu Asn
                405                 410                 415

cct gac att gag tgt gct gac tgc cca att ggt ttc tac aac gat ccg   1296
Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly Phe Tyr Asn Asp Pro
            420                 425                 430

cac gac ccc cgc agc tgc aag cca tgt ccc tgt cat aac ggg ttc agc   1344
His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys His Asn Gly Phe Ser
        435                 440                 445

tgc tca gtg atg ccg gag acg gag gag gtg gtg tgc aat aac tgc cct   1392
Cys Ser Val Met Pro Glu Thr Glu Glu Val Val Cys Asn Asn Cys Pro
    450                 455                 460

ccc ggg gtc acc ggt gcc cgc tgt gag ctc tgt gct gat ggc tac ttt   1440
Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys Ala Asp Gly Tyr Phe
465                 470                 475                 480

ggg gac ccc ttt ggt gaa cat ggc cca gtg agg cct tgt cag ccc tgt   1488
Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg Pro Cys Gln Pro Cys
                485                 490                 495

caa tgc aac aac aat gtg gac ccc agt gcc tct ggg aat tgt gac cgg   1536
Gln Cys Asn Asn Asn Val Asp Pro Ser Ala Ser Gly Asn Cys Asp Arg
            500                 505                 510

ctg aca ggc agg tgt ttg aag tgt atc cac aac aca gcc ggc atc tac   1584
Leu Thr Gly Arg Cys Leu Lys Cys Ile His Asn Thr Ala Gly Ile Tyr
        515                 520                 525

tgc gac cag tgc aaa gca ggc tac ttc ggg gac cca ttg gct ccc aac   1632
Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp Pro Leu Ala Pro Asn
    530                 535                 540

cca gca gac aag tgt cga gct tgc aac tgt aac ccc atg ggc tca gag   1680
Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Asn Pro Met Gly Ser Glu
545                 550                 555                 560

cct gta gga tgt cga agt gat ggc acc tgt gtt tgc aag cca gga ttt   1728
Pro Val Gly Cys Arg Ser Asp Gly Thr Cys Val Cys Lys Pro Gly Phe
                565                 570                 575

ggt ggc ccc aac tgt gag cat gga gca ttc agc tgt cca gct tgc tat   1776
Gly Gly Pro Asn Cys Glu His Gly Ala Phe Ser Cys Pro Ala Cys Tyr
            580                 585                 590

aat caa gtg aag att cag atg gat cag ttt atg cag cag ctt cag aga   1824
Asn Gln Val Lys Ile Gln Met Asp Gln Phe Met Gln Gln Leu Gln Arg
        595                 600                 605

atg gag gcc ctg att tca aag gct cag ggt ggt gat gga gta gta cct   1872
Met Glu Ala Leu Ile Ser Lys Ala Gln Gly Gly Asp Gly Val Val Pro
    610                 615                 620
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gat aca gag ctg gaa ggc agg atg cag cag gct gag cag gcc ctt cag   1920
Asp Thr Glu Leu Glu Gly Arg Met Gln Gln Ala Glu Gln Ala Leu Gln
625                 630                 635                 640

gac att ctg aga gat gcc cag att tca gaa ggt gct agc aga tcc ctt   1968
Asp Ile Leu Arg Asp Ala Gln Ile Ser Glu Gly Ala Ser Arg Ser Leu
                645                 650                 655

ggt ctc cag ttg gcc aag gtg agg agc caa gag aac agc tac cag agc   2016
Gly Leu Gln Leu Ala Lys Val Arg Ser Gln Glu Asn Ser Tyr Gln Ser
            660                 665                 670

cgc ctg gat gac ctc aag atg act gtg gaa aga gtt cgg gct ctg gga   2064
Arg Leu Asp Asp Leu Lys Met Thr Val Glu Arg Val Arg Ala Leu Gly
        675                 680                 685

agt cag tac cag aac cga gtt cgg gat act cac agg ctc atc act cag   2112
Ser Gln Tyr Gln Asn Arg Val Arg Asp Thr His Arg Leu Ile Thr Gln
    690                 695                 700

atg cag ctg agc ctg gca gaa agt gaa gct tcc ttg gga aac act aac   2160
Met Gln Leu Ser Leu Ala Glu Ser Glu Ala Ser Leu Gly Asn Thr Asn
705                 710                 715                 720

att cct gcc tca gac cac tac gtg ggg cca aat ggc ttt aaa agt ctg   2208
Ile Pro Ala Ser Asp His Tyr Val Gly Pro Asn Gly Phe Lys Ser Leu
                725                 730                 735

gct cag gag gcc aca aga tta gca gaa agc cac gtt gag tca gcc agt   2256
Ala Gln Glu Ala Thr Arg Leu Ala Glu Ser His Val Glu Ser Ala Ser
            740                 745                 750

aac atg gag caa ctg aca agg gaa act gag gac tat tcc aaa caa gcc   2304
Asn Met Glu Gln Leu Thr Arg Glu Thr Glu Asp Tyr Ser Lys Gln Ala
        755                 760                 765

ctc tca ctg gtg cgc aag gcc ctg cat gaa gga gtc gga agc gga agc   2352
Leu Ser Leu Val Arg Lys Ala Leu His Glu Gly Val Gly Ser Gly Ser
    770                 775                 780

ggt agc ccg gac ggt gct gtg gtg caa ggg ctt gtg gaa aaa ttg gag   2400
Gly Ser Pro Asp Gly Ala Val Val Gln Gly Leu Val Glu Lys Leu Glu
785                 790                 795                 800

aaa acc aag tcc ctg gcc cag cag ttg aca agg gag gcc act caa gcg   2448
Lys Thr Lys Ser Leu Ala Gln Gln Leu Thr Arg Glu Ala Thr Gln Ala
                805                 810                 815

gaa att gaa gca gat agg tct tat cag cac agt ctc cgc ctc ctg gat   2496
Glu Ile Glu Ala Asp Arg Ser Tyr Gln His Ser Leu Arg Leu Leu Asp
            820                 825                 830

tca gtg tct ccg ctt cag gga gtc agt gat cag tcc ttt cag gtg gaa   2544
Ser Val Ser Pro Leu Gln Gly Val Ser Asp Gln Ser Phe Gln Val Glu
        835                 840                 845

gaa gca aag agg atc aaa caa aaa gcg gat tca ctc tca agc ctg gta   2592
Glu Ala Lys Arg Ile Lys Gln Lys Ala Asp Ser Leu Ser Ser Leu Val
    850                 855                 860
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acc agg cat atg gat gag ttc aag cgt aca caa aag aat ctg gga aac   2640
Thr Arg His Met Asp Glu Phe Lys Arg Thr Gln Lys Asn Leu Gly Asn
865                 870                 875                 880

tgg aaa gaa gaa gca cag cag ctc tta cag aat gga aaa agt ggg aga   2688
Trp Lys Glu Glu Ala Gln Gln Leu Leu Gln Asn Gly Lys Ser Gly Arg
                885                 890                 895

gag aaa tca gat cag ctg ctt tcc cgt gcc aat ctt gct aaa agc aga   2736
Glu Lys Ser Asp Gln Leu Leu Ser Arg Ala Asn Leu Ala Lys Ser Arg
            900                 905                 910

gca caa gaa gca ctg agt atg ggc aat gcc act ttt tat gaa gtt gag   2784
Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr Phe Tyr Glu Val Glu
        915                 920                 925

agc atc ctt aaa aac ctc aga gag ttt gac ctg cag gtg gac aac aga   2832
Ser Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu Gln Val Asp Asn Arg
    930                 935                 940

aaa gca gaa gct gaa gaa gcc atg aag aga ctc tcc tac atc agc cag   2880
Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu Ser Tyr Ile Ser Gln
945                 950                 955                 960

aag gtt tca gat gcc agt gac aag acc cag caa gca gaa aga gcc ctg   2928
Lys Val Ser Asp Ala Ser Asp Lys Thr Gln Gln Ala Glu Arg Ala Leu
                965                 970                 975

ggg agc gct gct gct gat gca cag agg gca aag aat ggg gcc ggg gag   2976
Gly Ser Ala Ala Ala Asp Ala Gln Arg Ala Lys Asn Gly Ala Gly Glu
            980                 985                 990

gcc ctg gaa atc tcc agt gag att gaa cag gag att ggg agt ctg aac   3024
Ala Leu Glu Ile Ser Ser Glu Ile Glu Gln Glu Ile Gly Ser Leu Asn
        995                1000                1005

ttg gaa gcc aat gtg aca gca gat gga gcc ttg gcc atg gaa aag gga   3072
Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu Ala Met Glu Lys Gly
   1010                1015                1020

ctg gcc tct ctg aag agt gag atg agg gaa gtg gaa gga gag ctg gaa   3120
Leu Ala Ser Leu Lys Ser Glu Met Arg Glu Val Glu Gly Glu Leu Glu
1025                1030                1035                1040

agg aag gag ctg gag ttt gac acg aat atg gat gca gta cag atg gtg   3168
Arg Lys Glu Leu Glu Phe Asp Thr Asn Met Asp Ala Val Gln Met Val
                1045                1050                1055

att aca gaa gcc cag aag gtt gat acc aga gcc aag aac gct ggg gtt   3216
Ile Thr Glu Ala Gln Lys Val Asp Thr Arg Ala Lys Asn Ala Gly Val
            1060                1065                1070

aca atc caa gac aca ctc aac aca tta gac ggc ctc ctg cat ctg atg   3264
Thr Ile Gln Asp Thr Leu Asn Thr Leu Asp Gly Leu Leu His Leu Met
        1075                1080                1085

gac cag cct ctc agt gta gat gaa gag ggg ctg gtc tta ctg gag cag   3312
Asp Gln Pro Leu Ser Val Asp Glu Glu Gly Leu Val Leu Leu Glu Gln
   1090                1095                1100

aag ctt tcc cga gcc aag acc cag atc aac agc caa ctg cgg ccc atg   3360
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Lys Leu Ser Arg Ala Lys Thr Gln Ile Asn Ser Gln Leu Arg Pro Met
1105                1110                1115                1120

atg tca gag ctg gaa gag agg gca cgt cag cag agg ggc cac ctc cat   3408
Met Ser Glu Leu Glu Glu Arg Ala Arg Gln Gln Arg Gly His Leu His
                1125                1130                1135

ttg ctg gag aca agc ata gat ggg att ctg gct gat gtg aag aac ttg   3456
Leu Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp Val Lys Asn Leu
            1140                1145                1150

gag aac att agg gac aac ctg ccc cca ggc tgc tac aat acc cag gct   3504
Glu Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys Tyr Asn Thr Gln Ala
        1155                1160                1165

ctt gag caa cag tgaagctgcc ataaatattt ctcaactgag gttcttggga       3556
Leu Glu Gln Gln
    1170

tacagatctc agggctcggg agccatgtca tgtgagtggg tgggatgggg acatttgaac 3616

atgt                                                              3620


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Ile Phe Asp Arg Glu Leu His Arg Gln Thr Gly Asn Gly Phe Arg Cys
             20                  25                  30

Leu Asn Cys Asn Asp Asn Thr Asp Gly Ile His Cys Glu Lys Cys Lys
         35                  40                  45

Asn Gly Phe Tyr Arg His Arg Glu Arg Asp Arg Cys Leu Pro Cys Asn
     50                  55                  60

Cys Asn Ser Lys Gly Ser Leu Ser Ala Arg Cys Asp Asn Ser Gly Arg
 65                  70                  75                  80

Cys Ser Cys Lys Pro Gly Val Thr Gly Ala Arg Cys Asp Arg Cys Leu
                 85                  90                  95

Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys Thr Gln Asp Gln Arg
            100                 105                 110

Leu Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala Gly Ile Ala Gly Pro
        115                 120                 125

Cys Asp Ala Gly Arg Cys Val Cys Lys Pro Ala Val Thr Gly Glu Arg
    130                 135                 140

Cys Asp Gly Cys Arg Ser Gly Tyr Tyr Asn Leu Asp Gly Gly Asn Pro
145                 150                 155                 160

Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His Ser Ala Ser Cys Arg
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                165                 170                 175

Ser Ser Ala Glu Tyr Ser Val His Lys Ile Thr Ser Thr Phe His Gln
            180                 185                 190

Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn Gly Ser Pro Ala Lys
        195                 200                 205

Leu Gln Trp Ser Gln Arg His Gln Asp Val Phe Ser Ser Ala Gln Arg
    210                 215                 220

Leu Asp Pro Val Tyr Phe Val Ala Pro Ala Lys Phe Leu Gly Asn Gln
225                 230                 235                 240

Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp Tyr Arg Val Asp Arg
                245                 250                 255

Gly Gly Arg His Pro Ser Ala His Asp Val Ile Leu Glu Gly Ala Gly
            260                 265                 270

Leu Arg Ile Thr Ala Pro Leu Met Pro Leu Gly Lys Thr Leu Pro Cys
        275                 280                 285

Gly Leu Thr Lys Thr Tyr Thr Phe Arg Leu Asn Glu His Pro Ser Asn
    290                 295                 300

Asn Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr Arg Arg Leu Leu Arg
305                 310                 315                 320

Asn Leu Thr Ala Leu Arg Ile Arg Ala Thr Tyr Gly Glu Tyr Ser Thr
                325                 330                 335

Gly Tyr Ile Asp Asn Val Thr Leu Ile Ser Ala Arg Pro Val Ser Gly
            340                 345                 350

Ala Pro Ala Pro Trp Val Glu Gln Cys Ile Cys Pro Val Gly Tyr Lys
        355                 360                 365

Gly Gln Phe Cys Gln Asp Cys Ala Ser Gly Tyr Lys Arg Asp Ser Ala
    370                 375                 380

Arg Leu Gly Pro Phe Gly Thr Cys Ile Pro Cys Asn Cys Gln Gly Gly
385                 390                 395                 400

Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr Ser Gly Asp Glu Asn
                405                 410                 415

Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly Phe Tyr Asn Asp Pro
            420                 425                 430

His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys His Asn Gly Phe Ser
        435                 440                 445

Cys Ser Val Met Pro Glu Thr Glu Glu Val Val Cys Asn Asn Cys Pro
    450                 455                 460

Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys Ala Asp Gly Tyr Phe
465                 470                 475                 480

Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg Pro Cys Gln Pro Cys
                485                 490                 495
```

```
Gln Cys Asn Asn Asn Val Asp Pro Ser Ala Ser Gly Asn Cys Asp Arg
            500                 505                 510

Leu Thr Gly Arg Cys Leu Lys Cys Ile His Asn Thr Ala Gly Ile Tyr
        515                 520                 525

Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp Pro Leu Ala Pro Asn
    530                 535                 540

Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Asn Pro Met Gly Ser Glu
545                 550                 555                 560

Pro Val Gly Cys Arg Ser Asp Gly Thr Cys Val Cys Lys Pro Gly Phe
                565                 570                 575

Gly Gly Pro Asn Cys Glu His Gly Ala Phe Ser Cys Pro Ala Cys Tyr
            580                 585                 590

Asn Gln Val Lys Ile Gln Met Asp Gln Phe Met Gln Gln Leu Gln Arg
        595                 600                 605

Met Glu Ala Leu Ile Ser Lys Ala Gln Gly Gly Asp Gly Val Val Pro
    610                 615                 620

Asp Thr Glu Leu Glu Gly Arg Met Gln Gln Ala Glu Gln Ala Leu Gln
625                 630                 635                 640

Asp Ile Leu Arg Asp Ala Gln Ile Ser Glu Gly Ala Ser Arg Ser Leu
                645                 650                 655

Gly Leu Gln Leu Ala Lys Val Arg Ser Gln Glu Asn Ser Tyr Gln Ser
            660                 665                 670

Arg Leu Asp Asp Leu Lys Met Thr Val Glu Arg Val Arg Ala Leu Gly
        675                 680                 685

Ser Gln Tyr Gln Asn Arg Val Arg Asp Thr His Arg Leu Ile Thr Gln
    690                 695                 700

Met Gln Leu Ser Leu Ala Glu Ser Glu Ala Ser Leu Gly Asn Thr Asn
705                 710                 715                 720

Ile Pro Ala Ser Asp His Tyr Val Gly Pro Asn Gly Phe Lys Ser Leu
                725                 730                 735

Ala Gln Glu Ala Thr Arg Leu Ala Glu Ser His Val Glu Ser Ala Ser
            740                 745                 750

Asn Met Glu Gln Leu Thr Arg Glu Thr Glu Asp Tyr Ser Lys Gln Ala
        755                 760                 765

Leu Ser Leu Val Arg Lys Ala Leu His Glu Gly Val Gly Ser Gly Ser
    770                 775                 780

Gly Ser Pro Asp Gly Ala Val Val Gln Gly Leu Val Glu Lys Leu Glu
785                 790                 795                 800

Lys Thr Lys Ser Leu Ala Gln Gln Leu Thr Arg Glu Ala Thr Gln Ala
                805                 810                 815
```

```
Glu Ile Glu Ala Asp Arg Ser Tyr Gln His Ser Leu Arg Leu Leu Asp
            820                 825                 830

Ser Val Ser Pro Leu Gln Gly Val Ser Asp Gln Ser Phe Gln Val Glu
        835                 840                 845

Glu Ala Lys Arg Ile Lys Gln Lys Ala Asp Ser Leu Ser Ser Leu Val
    850                 855                 860

Thr Arg His Met Asp Glu Phe Lys Arg Thr Gln Lys Asn Leu Gly Asn
865                 870                 875                 880

Trp Lys Glu Glu Ala Gln Gln Leu Leu Gln Asn Gly Lys Ser Gly Arg
                885                 890                 895

Glu Lys Ser Asp Gln Leu Leu Ser Arg Ala Asn Leu Ala Lys Ser Arg
            900                 905                 910

Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr Phe Tyr Glu Val Glu
        915                 920                 925

Ser Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu Gln Val Asp Asn Arg
    930                 935                 940

Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu Ser Tyr Ile Ser Gln
945                 950                 955                 960

Lys Val Ser Asp Ala Ser Asp Lys Thr Gln Gln Ala Glu Arg Ala Leu
                965                 970                 975

Gly Ser Ala Ala Ala Asp Ala Gln Arg Ala Lys Asn Gly Ala Gly Glu
            980                 985                 990

Ala Leu Glu Ile Ser Ser Glu Ile Glu Gln Glu Ile Gly Ser Leu Asn
        995                1000                1005

Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu Ala Met Glu Lys Gly
   1010                1015                1020

Leu Ala Ser Leu Lys Ser Glu Met Arg Glu Val Glu Gly Glu Leu Glu
1025                1030                1035                1040

Arg Lys Glu Leu Glu Phe Asp Thr Asn Met Asp Ala Val Gln Met Val
                1045                1050                1055

Ile Thr Glu Ala Gln Lys Val Asp Thr Arg Ala Lys Asn Ala Gly Val
            1060                1065                1070

Thr Ile Gln Asp Thr Leu Asn Thr Leu Asp Gly Leu Leu His Leu Met
        1075                1080                1085

Asp Gln Pro Leu Ser Val Asp Glu Glu Gly Leu Val Leu Leu Glu Gln
   1090                1095                1100

Lys Leu Ser Arg Ala Lys Thr Gln Ile Asn Ser Gln Leu Arg Pro Met
1105                1110                1115                1120

Met Ser Glu Leu Glu Glu Arg Ala Arg Gln Gln Arg Gly His Leu His
                1125                1130                1135

Leu Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp Val Lys Asn Leu
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Leu Glu Gln Gln
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Leu Ser Cys Cys Leu Gly Val Ala Leu Leu Leu Pro Ala Ser Gln Ala
                10                  15                  20

acc tcc agg agg gaa gtc tgt gat tgc aat ggg aag tcc agg caa tgt   150
Thr Ser Arg Arg Glu Val Cys Asp Cys Asn Gly Lys Ser Arg Gln Cys
            25                  30                  35

gtc ttt gat cag gag ctc cat cga caa gca ggc agc ggg ttc cgt tgc   198
Val Phe Asp Gln Glu Leu His Arg Gln Ala Gly Ser Gly Phe Arg Cys
        40                  45                  50

ctc aac tgc aat gac aat aca gcg ggg gtt cac tgc gag cgg tcg agg   246
Leu Asn Cys Asn Asp Asn Thr Ala Gly Val His Cys Glu Arg Ser Arg
    55                  60                  65

gag ggg ttt tac cag cat cag agc aag agc cgc tgc cta ccc tgc aac   294
Glu Gly Phe Tyr Gln His Gln Ser Lys Ser Arg Cys Leu Pro Cys Asn
70                  75                  80                  85

tgc cac tca aag ggt tcc ctc agt gct gga tgt gac aac tct gga caa   342
Cys His Ser Lys Gly Ser Leu Ser Ala Gly Cys Asp Asn Ser Gly Gln
                90                  95                  100

tgc agg tgt aag cca ggt gtg aca gga caa aga tgt gac cag tgt cag   390
Cys Arg Cys Lys Pro Gly Val Thr Gly Gln Arg Cys Asp Gln Cys Gln
            105                 110                 115

cca ggc ttc cat atg ctc acc gat gct gga tgc acc cga gac cag ggg   438
Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys Thr Arg Asp Gln Gly
        120                 125                 130

caa cta gat tcc aag tgt gac tgt gac cca gct ggc atc tct gga ccc   486
Gln Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala Gly Ile Ser Gly Pro
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    135                 140                 145

tgt gat tct ggc cga tgt gtc tgc aaa cca gcc gtc act gga gag cgc   534
Cys Asp Ser Gly Arg Cys Val Cys Lys Pro Ala Val Thr Gly Glu Arg
150                 155                 160                 165

tgt gat agg tgc cga cca cgt gac tat cat ctg gac cgg gca aac cct   582
Cys Asp Arg Cys Arg Pro Arg Asp Tyr His Leu Asp Arg Ala Asn Pro
                170                 175                 180

gag ggc tgt acc cag tgt ttc tgc tat ggg cat tca gcc agc tgc cac   630
Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His Ser Ala Ser Cys His
            185                 190                 195

gcc tct gcc gac ttc agt gtc cac aaa atc act tca act ttc agt cag   678
Ala Ser Ala Asp Phe Ser Val His Lys Ile Thr Ser Thr Phe Ser Gln
        200                 205                 210

gat gtg gat ggt tgg aag gcg gtt cag aga aac ggg gca cct gca aaa   726
Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn Gly Ala Pro Ala Lys
    215                 220                 225

ctc cac tgg tca cag cgc cat cgg gac gtg ttt agt tct gcc cga aga   774
Leu His Trp Ser Gln Arg His Arg Asp Val Phe Ser Ser Ala Arg Arg
230                 235                 240                 245

tca gac ccc gtc tat ttc gtg gcc cct gcc aaa ttc ctc ggt aac cag   822
Ser Asp Pro Val Tyr Phe Val Ala Pro Ala Lys Phe Leu Gly Asn Gln
                250                 255                 260

caa gtg agt tac ggg cag agc ctg tct ttt gac tac cgc gtg gac aga   870
Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp Tyr Arg Val Asp Arg
            265                 270                 275

gga ggt aga cag ccg tct gcc tac gat gtg atc ctg gaa ggt gct ggt   918
Gly Gly Arg Gln Pro Ser Ala Tyr Asp Val Ile Leu Glu Gly Ala Gly
        280                 285                 290

cta cag atc aga gct cct ctg atg gct cca ggc aag aca ctt cct tgt   966
Leu Gln Ile Arg Ala Pro Leu Met Ala Pro Gly Lys Thr Leu Pro Cys
    295                 300                 305

ggg atc aca aag act tac aca ttc aga ctg aat gaa cat cca agc agt   1014
Gly Ile Thr Lys Thr Tyr Thr Phe Arg Leu Asn Glu His Pro Ser Ser
310                 315                 320                 325

cac tgg agt ccc cag ctg agt tat ttc gaa tat cga agg tta ctg cgg   1062
His Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr Arg Arg Leu Leu Arg
                330                 335                 340

aac ctc aca gcc ctc ctg atg atc cga gct acg tac gga gaa tat agt   1110
Asn Leu Thr Ala Leu Leu Met Ile Arg Ala Thr Tyr Gly Glu Tyr Ser
            345                 350                 355

aca ggg tac att gat aac gtg acc ctg gtt tca gcc cgc cct gtc ctt   1158
Thr Gly Tyr Ile Asp Asn Val Thr Leu Val Ser Ala Arg Pro Val Leu
        360                 365                 370

gga gcc cca gcc cct tgg gtt gaa cgt tgt gta tgc ctg ctg ggg tac   1206
Gly Ala Pro Ala Pro Trp Val Glu Arg Cys Val Cys Leu Leu Gly Tyr
    375                 380                 385
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aag gga caa ttc tgc cag gaa tgt gct tct ggt tac aaa aga gat tcg   1254
Lys Gly Gln Phe Cys Gln Glu Cys Ala Ser Gly Tyr Lys Arg Asp Ser
390                 395                 400                 405

gca aga ttg ggc gct ttt ggc gcc tgt gtt ccc tgt aac tgc caa ggg   1302
Ala Arg Leu Gly Ala Phe Gly Ala Cys Val Pro Cys Asn Cys Gln Gly
                410                 415                 420

gag ggg gcc tgt gat cca gac acg gga gat tgc tac tcg ggg gac gag   1350
Glu Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr Ser Gly Asp Glu
            425                 430                 435

aat cct gac att gag tgt gct gac tgt ccc atc ggt ttc tac aat gac   1398
Asn Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly Phe Tyr Asn Asp
        440                 445                 450

cca cat gac ccc cgc agc tgc aag cca tgt ccc tgt cac aat ggg ttc   1446
Pro His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys His Asn Gly Phe
    455                 460                 465

agc tgt tca gtg atg cct gag aca gag gag gtg gtg tgt aac aac tgt   1494
Ser Cys Ser Val Met Pro Glu Thr Glu Glu Val Val Cys Asn Asn Cys
470                 475                 480                 485

ccc cct ggg gtc aca ggt gcc cgc tgt gag ctc tgt gct gat ggc ttc   1542
Pro Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys Ala Asp Gly Phe
                490                 495                 500

ttt ggg gat ccc ttt ggg gaa cat ggc cca gtg agg cct tgt caa cgc   1590
Phe Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg Pro Cys Gln Arg
            505                 510                 515

tgc caa tgc aac aac aac gtg gac ccc aat gcc tct ggg aac tgt gac   1638
Cys Gln Cys Asn Asn Asn Val Asp Pro Asn Ala Ser Gly Asn Cys Asp
        520                 525                 530

cag ttg aca ggc aga tgc ttg aaa tgt atc tac aac acg gcc ggt gtc   1686
Gln Leu Thr Gly Arg Cys Leu Lys Cys Ile Tyr Asn Thr Ala Gly Val
    535                 540                 545

tac tgt gac cag tgc aaa gca ggt tac ttt gga gac cca ttg gct ccc   1734
Tyr Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp Pro Leu Ala Pro
550                 555                 560                 565

aac cca gca gac aag tgt cga gct tgc aac tgc agc ccc atg ggt gcg   1782
Asn Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Ser Pro Met Gly Ala
                570                 575                 580

gag cct gga gag tgt cga ggt gat ggc agc tgt gtt tgc aag cca ggc   1830
Glu Pro Gly Glu Cys Arg Gly Asp Gly Ser Cys Val Cys Lys Pro Gly
            585                 590                 595

ttt ggc gcc ttc aac tgt gat cac gca gcc cta acc agt tgt cct gct   1878
Phe Gly Ala Phe Asn Cys Asp His Ala Ala Leu Thr Ser Cys Pro Ala
        600                 605                 610

tgc tac aat caa gtg aag att cag atg gac cag ttt acc cag cag ctc   1926
Cys Tyr Asn Gln Val Lys Ile Gln Met Asp Gln Phe Thr Gln Gln Leu
    615                 620                 625
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cag agc ctg gag gcc ctg gtt tca aag gct cag ggt ggt ggt ggt ggt   1974
Gln Ser Leu Glu Ala Leu Val Ser Lys Ala Gln Gly Gly Gly Gly Gly
630                 635                 640                 645

ggt aca gtc cca gtg cag ctg gaa ggc agg atc gag cag gct gag cag   2022
Gly Thr Val Pro Val Gln Leu Glu Gly Arg Ile Glu Gln Ala Glu Gln
                650                 655                 660

gcc ctt cag gac att ctg gga gaa gct cag att tca gaa ggg gca atg   2070
Ala Leu Gln Asp Ile Leu Gly Glu Ala Gln Ile Ser Glu Gly Ala Met
            665                 670                 675

aga gcc gtt gct gtc cgg ctg gcc aag gca agg agc caa gag aac gac   2118
Arg Ala Val Ala Val Arg Leu Ala Lys Ala Arg Ser Gln Glu Asn Asp
        680                 685                 690

tac aag acc cgc ctg gat gac ctc aag atg act gca gaa agg atc cgg   2166
Tyr Lys Thr Arg Leu Asp Asp Leu Lys Met Thr Ala Glu Arg Ile Arg
    695                 700                 705

gcc ctg ggc agt cag cat cag aac aga gtt cag gat acg agc aga ctc   2214
Ala Leu Gly Ser Gln His Gln Asn Arg Val Gln Asp Thr Ser Arg Leu
710                 715                 720                 725

atc tct cag atg cgc ctg agt ctg gca gga agc gaa gct ctc ttg gaa   2262
Ile Ser Gln Met Arg Leu Ser Leu Ala Gly Ser Glu Ala Leu Leu Glu
                730                 735                 740

aac act aat atc cat tct tct gag cac tac gtg ggg ccg aat gat ttt   2310
Asn Thr Asn Ile His Ser Ser Glu His Tyr Val Gly Pro Asn Asp Phe
            745                 750                 755

aaa agt ctg gct cag gag gct aca aga aag gca gac agc cac gct gag   2358
Lys Ser Leu Ala Gln Glu Ala Thr Arg Lys Ala Asp Ser His Ala Glu
        760                 765                 770

tca gct aac gca atg aag caa cta gca agg gaa act gag gac tac tcc   2406
Ser Ala Asn Ala Met Lys Gln Leu Ala Arg Glu Thr Glu Asp Tyr Ser
    775                 780                 785

aaa caa gca ctt tca ttg gcc cgc aag ctc ttg agt gga gga ggc gga   2454
Lys Gln Ala Leu Ser Leu Ala Arg Lys Leu Leu Ser Gly Gly Gly Gly
790                 795                 800                 805

agt ggc tct tgg gac agc tcc gtg gta caa ggt ctt atg gga aaa tta   2502
Ser Gly Ser Trp Asp Ser Ser Val Val Gln Gly Leu Met Gly Lys Leu
                810                 815                 820

gag aaa acc aag tcc ctg agc cag cag ctg tca ttg gag ggc acc caa   2550
Glu Lys Thr Lys Ser Leu Ser Gln Gln Leu Ser Leu Glu Gly Thr Gln
            825                 830                 835

gcc gac att gaa gct gat agg tcg tat cag cac agt ctc cgc ctc ctg   2598
Ala Asp Ile Glu Ala Asp Arg Ser Tyr Gln His Ser Leu Arg Leu Leu
        840                 845                 850

gat tct gcc tct cag ctt cag gga gtc agt gat ctg tcc ttt cag gtg   2646
Asp Ser Ala Ser Gln Leu Gln Gly Val Ser Asp Leu Ser Phe Gln Val
    855                 860                 865

gaa gca aag agg atc aga caa aag gct gat tct ctc tca aac ctg gtg   2694
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Glu Ala Lys Arg Ile Arg Gln Lys Ala Asp Ser Leu Ser Asn Leu Val
870                 875                 880                 885

acc aga caa acg gat gca ttc acg cgt gtg cga aac aat ctg ggg aac   2742
Thr Arg Gln Thr Asp Ala Phe Thr Arg Val Arg Asn Asn Leu Gly Asn
                890                 895                 900

tgg gaa aaa gaa aca cgg cag ctt tta cag act gga aag gat agg aga   2790
Trp Glu Lys Glu Thr Arg Gln Leu Leu Gln Thr Gly Lys Asp Arg Arg
            905                 910                 915

cag act tca gat cag ctg ctt tcc cgt gcc aac ctt gct aaa aac aga   2838
Gln Thr Ser Asp Gln Leu Leu Ser Arg Ala Asn Leu Ala Lys Asn Arg
        920                 925                 930

gcc caa gaa gcg cta agt atg ggc aat gcc act ttt tat gaa gtt gag   2886
Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr Phe Tyr Glu Val Glu
    935                 940                 945

aac atc ctg aag aac ctc cga gag ttt gat ctg cag gtt gaa gac aga   2934
Asn Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu Gln Val Glu Asp Arg
950                 955                 960                 965

aaa gca gag gct gaa gag gcc atg aag aga ctc tcc tct att agc cag   2982
Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu Ser Ser Ile Ser Gln
                970                 975                 980

aag gtt gcg gat gcc agt gac aag acc cag caa gca gaa acg gcc ctg   3030
Lys Val Ala Asp Ala Ser Asp Lys Thr Gln Gln Ala Glu Thr Ala Leu
            985                 990                 995

ggg agc gcc act gcc gac acc caa cgg gca aag aac gca gct agg gag   3078
Gly Ser Ala Thr Ala Asp Thr Gln Arg Ala Lys Asn Ala Ala Arg Glu
       1000                1005                1010

gcc ctg gag atc agc agc gag ata gag ctg gag ata ggg agt ctg aac   3126
Ala Leu Glu Ile Ser Ser Glu Ile Glu Leu Glu Ile Gly Ser Leu Asn
   1015                1020                1025

ttg gaa gct aat gtg aca gca gat ggg gcc ttg gcc atg gag aaa ggg   3174
Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu Ala Met Glu Lys Gly
1030                1035                1040                1045

act gcc act ctg aag agc gag atg aga gag atg att gag ctg gcc aga   3222
Thr Ala Thr Leu Lys Ser Glu Met Arg Glu Met Ile Glu Leu Ala Arg
               1050                1055                1060

aag gag ctg gag ttt gac acg gat aag gac acg gtg cag ctg gtg att   3270
Lys Glu Leu Glu Phe Asp Thr Asp Lys Asp Thr Val Gln Leu Val Ile
           1065                1070                1075

act gaa gcc cag caa gct gat gcc aga gcc acg agt gcc gga gtt acc   3318
Thr Glu Ala Gln Gln Ala Asp Ala Arg Ala Thr Ser Ala Gly Val Thr
       1080                1085                1090

atc caa gac acr ctc aac aca ttg gac ggc atc cta cac ctc ata gac   3366
Ile Gln Asp Xaa Leu Asn Thr Leu Asp Gly Ile Leu His Leu Ile Asp
   1095                1100                1105

cag cct ggc agt gtg gat gaa gaa ggg atg atg cta tta gaa caa ggg   3414
Gln Pro Gly Ser Val Asp Glu Glu Gly Met Met Leu Leu Glu Gln Gly
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ctt ttc caa gcc aag acc cag atc aac agt cga ctt cgg ccc ttg atg   3462
Leu Phe Gln Ala Lys Thr Gln Ile Asn Ser Arg Leu Arg Pro Leu Met
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tct gac ctg gag gag agg gtg cgt cgg cag agg aac cac ctc cat ctg   3510
Ser Asp Leu Glu Glu Arg Val Arg Arg Gln Arg Asn His Leu His Leu
            1145                1150                1155

ctg gag act agc ata gat gga att ctt gct gat gtg aag aac ctg gag   3558
Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp Val Lys Asn Leu Glu
        1160                1165                1170

aac att cga gac aac ctg ccc cca ggc tgc tac aat acc caa gct ctt   3606
Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys Tyr Asn Thr Gln Ala Leu
    1175                1180                1185

gag caa cag tgaagttgtc atagagattt gtccactgtt gtgaaaggac           3655
Glu Gln Gln
1190

acagacctca ggggtcagga gccatctcgt gtggatgggc tgtgctcagg ctatctgaac 3715

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             20                  25                  30

Lys Ser Arg Gln Cys Val Phe Asp Gln Glu Leu His Arg Gln Ala Gly
         35                  40                  45

Ser Gly Phe Arg Cys Leu Asn Cys Asn Asp Asn Thr Ala Gly Val His
     50                  55                  60

Cys Glu Arg Ser Arg Glu Gly Phe Tyr Gln His Gln Ser Lys Ser Arg
 65                  70                  75                  80

Cys Leu Pro Cys Asn Cys His Ser Lys Gly Ser Leu Ser Ala Gly Cys
                 85                  90                  95

Asp Asn Ser Gly Gln Cys Arg Cys Lys Pro Gly Val Thr Gly Gln Arg
            100                 105                 110

Cys Asp Gln Cys Gln Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys
        115                 120                 125

Thr Arg Asp Gln Gly Gln Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala
    130                 135                 140

Gly Ile Ser Gly Pro Cys Asp Ser Gly Arg Cys Val Cys Lys Pro Ala
145                 150                 155                 160

Val Thr Gly Glu Arg Cys Asp Arg Cys Arg Pro Arg Asp Tyr His Leu
                165                 170                 175

Asp Arg Ala Asn Pro Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His
            180                 185                 190

Ser Ala Ser Cys His Ala Ser Ala Asp Phe Ser Val His Lys Ile Thr
        195                 200                 205

Ser Thr Phe Ser Gln Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn
    210                 215                 220
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Gly Ala Pro Ala Lys Leu His Trp Ser Gln Arg His Arg Asp Val Phe
225                 230                 235                 240

Ser Ser Ala Arg Arg Ser Asp Pro Val Tyr Phe Val Ala Pro Ala Lys
                245                 250                 255

Phe Leu Gly Asn Gln Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp
            260                 265                 270

Tyr Arg Val Asp Arg Gly Gly Arg Gln Pro Ser Ala Tyr Asp Val Ile
        275                 280                 285

Leu Glu Gly Ala Gly Leu Gln Ile Arg Ala Pro Leu Met Ala Pro Gly
    290                 295                 300

Lys Thr Leu Pro Cys Gly Ile Thr Lys Thr Tyr Thr Phe Arg Leu Asn
305                 310                 315                 320

Glu His Pro Ser Ser His Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr
                325                 330                 335

Arg Arg Leu Leu Arg Asn Leu Thr Ala Leu Leu Met Ile Arg Ala Thr
            340                 345                 350

Tyr Gly Glu Tyr Ser Thr Gly Tyr Ile Asp Asn Val Thr Leu Val Ser
        355                 360                 365

Ala Arg Pro Val Leu Gly Ala Pro Ala Pro Trp Val Glu Arg Cys Val
    370                 375                 380

Cys Leu Leu Gly Tyr Lys Gly Gln Phe Cys Gln Glu Cys Ala Ser Gly
385                 390                 395                 400

Tyr Lys Arg Asp Ser Ala Arg Leu Gly Ala Phe Gly Ala Cys Val Pro
                405                 410                 415

Cys Asn Cys Gln Gly Glu Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys
            420                 425                 430

Tyr Ser Gly Asp Glu Asn Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile
        435                 440                 445

Gly Phe Tyr Asn Asp Pro His Asp Pro Arg Ser Cys Lys Pro Cys Pro
    450                 455                 460

Cys His Asn Gly Phe Ser Cys Ser Val Met Pro Glu Thr Glu Glu Val
465                 470                 475                 480

Val Cys Asn Asn Cys Pro Pro Gly Val Thr Gly Ala Arg Cys Glu Leu
                485                 490                 495

Cys Ala Asp Gly Phe Phe Gly Asp Pro Phe Gly Glu His Gly Pro Val
            500                 505                 510

Arg Pro Cys Gln Arg Cys Gln Cys Asn Asn Asn Val Asp Pro Asn Ala
        515                 520                 525

Ser Gly Asn Cys Asp Gln Leu Thr Gly Arg Cys Leu Lys Cys Ile Tyr
    530                 535                 540
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Asn Thr Ala Gly Val Tyr Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly
545                 550                 555                 560

Asp Pro Leu Ala Pro Asn Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys
                565                 570                 575

Ser Pro Met Gly Ala Glu Pro Gly Glu Cys Arg Gly Asp Gly Ser Cys
            580                 585                 590

Val Cys Lys Pro Gly Phe Gly Ala Phe Asn Cys Asp His Ala Ala Leu
        595                 600                 605

Thr Ser Cys Pro Ala Cys Tyr Asn Gln Val Lys Ile Gln Met Asp Gln
    610                 615                 620

Phe Thr Gln Gln Leu Gln Ser Leu Glu Ala Leu Val Ser Lys Ala Gln
625                 630                 635                 640

Gly Gly Gly Gly Gly Gly Thr Val Pro Val Gln Leu Glu Gly Arg Ile
                645                 650                 655

Glu Gln Ala Glu Gln Ala Leu Gln Asp Ile Leu Gly Glu Ala Gln Ile
            660                 665                 670

Ser Glu Gly Ala Met Arg Ala Val Ala Val Arg Leu Ala Lys Ala Arg
        675                 680                 685

Ser Gln Glu Asn Asp Tyr Lys Thr Arg Leu Asp Asp Leu Lys Met Thr
    690                 695                 700

Ala Glu Arg Ile Arg Ala Leu Gly Ser Gln His Gln Asn Arg Val Gln
705                 710                 715                 720

Asp Thr Ser Arg Leu Ile Ser Gln Met Arg Leu Ser Leu Ala Gly Ser
                725                 730                 735

Glu Ala Leu Leu Glu Asn Thr Asn Ile His Ser Ser Glu His Tyr Val
            740                 745                 750

Gly Pro Asn Asp Phe Lys Ser Leu Ala Gln Glu Ala Thr Arg Lys Ala
        755                 760                 765

Asp Ser His Ala Glu Ser Ala Asn Ala Met Lys Gln Leu Ala Arg Glu
    770                 775                 780

Thr Glu Asp Tyr Ser Lys Gln Ala Leu Ser Leu Ala Arg Lys Leu Leu
785                 790                 795                 800

Ser Gly Gly Gly Gly Ser Gly Ser Trp Asp Ser Ser Val Val Gln Gly
                805                 810                 815

Leu Met Gly Lys Leu Glu Lys Thr Lys Ser Leu Ser Gln Gln Leu Ser
            820                 825                 830

Leu Glu Gly Thr Gln Ala Asp Ile Glu Ala Asp Arg Ser Tyr Gln His
        835                 840                 845

Ser Leu Arg Leu Leu Asp Ser Ala Ser Gln Leu Gln Gly Val Ser Asp
    850                 855                 860

Leu Ser Phe Gln Val Glu Ala Lys Arg Ile Arg Gln Lys Ala Asp Ser
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865 870 875 880

Leu Ser Asn Leu Val Thr Arg Gln Thr Asp Ala Phe Thr Arg Val Arg
885 890 895

Asn Asn Leu Gly Asn Trp Glu Lys Glu Thr Arg Gln Leu Leu Gln Thr
900 905 910

Gly Lys Asp Arg Arg Gln Thr Ser Asp Gln Leu Leu Ser Arg Ala Asn
915 920 925

Leu Ala Lys Asn Arg Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr
930 935 940

Phe Tyr Glu Val Glu Asn Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu
945 950 955 960

Gln Val Glu Asp Arg Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu
965 970 975

Ser Ser Ile Ser Gln Lys Val Ala Asp Ala Ser Asp Lys Thr Gln Gln
980 985 990

Ala Glu Thr Ala Leu Gly Ser Ala Thr Ala Asp Thr Gln Arg Ala Lys
995 1000 1005

Asn Ala Ala Arg Glu Ala Leu Glu Ile Ser Ser Glu Ile Glu Leu Glu
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Ile Gly Ser Leu Asn Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu
025 1030 1035 1040

Ala Met Glu Lys Gly Thr Ala Thr Leu Lys Ser Glu Met Arg Glu Met
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Ile Glu Leu Ala Arg Lys Glu Leu Glu Phe Asp Thr Asp Lys Asp Thr
1060 1065 1070

Val Gln Leu Val Ile Thr Glu Ala Gln Gln Ala Asp Ala Arg Ala Thr
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Ser Ala Gly Val Thr Ile Gln Asp Xaa Leu Asn Thr Leu Asp Gly Ile
1090 1095 1100

Leu His Leu Ile Asp Gln Pro Gly Ser Val Asp Glu Glu Gly Met Met
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Leu Leu Glu Gln Gly Leu Phe Gln Ala Lys Thr Gln Ile Asn Ser Arg
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Leu Arg Pro Leu Met Ser Asp Leu Glu Glu Arg Val Arg Arg Gln Arg
1140 1145 1150

Asn His Leu His Leu Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp
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Val Lys Asn Leu Glu Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys Tyr
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Asn Thr Gln Ala Leu Glu Gln Gln
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Thr Ser Arg Arg Glu Val Cys Asp Cys Asn Gly Lys Ser Arg Gln Cys
  1               5                  10                  15

gtc ttt gat cag gag ctc cat cga caa gca ggc agc ggg ttc cgt tgc   96
Val Phe Asp Gln Glu Leu His Arg Gln Ala Gly Ser Gly Phe Arg Cys
             20                  25                  30

ctc aac tgc aat gac aat aca gcg ggg gtt cac tgc gag cgg tcg agg   144
Leu Asn Cys Asn Asp Asn Thr Ala Gly Val His Cys Glu Arg Ser Arg
         35                  40                  45

gag ggg ttt tac cag cat cag agc aag agc cgc tgc cta ccc tgc aac   192
Glu Gly Phe Tyr Gln His Gln Ser Lys Ser Arg Cys Leu Pro Cys Asn
     50                  55                  60

tgc cac tca aag ggt tcc ctc agt gct gga tgt gac aac tct gga caa   240
Cys His Ser Lys Gly Ser Leu Ser Ala Gly Cys Asp Asn Ser Gly Gln
 65                  70                  75                  80

tgc agg tgt aag cca ggt gtg aca gga caa aga tgt gac cag tgt cag   288
Cys Arg Cys Lys Pro Gly Val Thr Gly Gln Arg Cys Asp Gln Cys Gln
                 85                  90                  95

cca ggc ttc cat atg ctc acc gat gct gga tgc acc cga gac cag ggg   336
Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys Thr Arg Asp Gln Gly
            100                 105                 110

caa cta gat tcc aag tgt gac tgt gac cca gct ggc atc tct gga ccc   384
Gln Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala Gly Ile Ser Gly Pro
        115                 120                 125

tgt gat tct ggc cga tgt gtc tgc aaa cca gcc gtc act gga gag cgc   432
Cys Asp Ser Gly Arg Cys Val Cys Lys Pro Ala Val Thr Gly Glu Arg
    130                 135                 140

tgt gat agg tgc cga cca cgt gac tat cat ctg gac cgg gca aac cct   480
Cys Asp Arg Cys Arg Pro Arg Asp Tyr His Leu Asp Arg Ala Asn Pro
145                 150                 155                 160

gag ggc tgt acc cag tgt ttc tgc tat ggg cat tca gcc agc tgc cac   528
Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His Ser Ala Ser Cys His
                165                 170                 175

gcc tct gcc gac ttc agt gtc cac aaa atc act tca act ttc agt cag   576
Ala Ser Ala Asp Phe Ser Val His Lys Ile Thr Ser Thr Phe Ser Gln
            180                 185                 190

gat gtg gat ggt tgg aag gcg gtt cag aga aac ggg gca cct gca aaa   624
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Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn Gly Ala Pro Ala Lys
        195                 200                 205

ctc cac tgg tca cag cgc cat cgg gac gtg ttt agt tct gcc cga aga   672
Leu His Trp Ser Gln Arg His Arg Asp Val Phe Ser Ser Ala Arg Arg
    210                 215                 220

tca gac ccc gtc tat ttc gtg gcc cct gcc aaa ttc ctc ggt aac cag   720
Ser Asp Pro Val Tyr Phe Val Ala Pro Ala Lys Phe Leu Gly Asn Gln
225                 230                 235                 240

caa gtg agt tac ggg cag agc ctg tct ttt gac tac cgc gtg gac aga   768
Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp Tyr Arg Val Asp Arg
                245                 250                 255

gga ggt aga cag ccg tct gcc tac gat gtg atc ctg gaa ggt gct ggt   816
Gly Gly Arg Gln Pro Ser Ala Tyr Asp Val Ile Leu Glu Gly Ala Gly
            260                 265                 270

cta cag atc aga gct cct ctg atg gct cca ggc aag aca ctt cct tgt   864
Leu Gln Ile Arg Ala Pro Leu Met Ala Pro Gly Lys Thr Leu Pro Cys
        275                 280                 285

ggg atc aca aag act tac aca ttc aga ctg aat gaa cat cca agc agt   912
Gly Ile Thr Lys Thr Tyr Thr Phe Arg Leu Asn Glu His Pro Ser Ser
    290                 295                 300

cac tgg agt ccc cag ctg agt tat ttc gaa tat cga agg tta ctg cgg   960
His Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr Arg Arg Leu Leu Arg
305                 310                 315                 320

aac ctc aca gcc ctc ctg atg atc cga gct acg tac gga gaa tat agt  1008
Asn Leu Thr Ala Leu Leu Met Ile Arg Ala Thr Tyr Gly Glu Tyr Ser
                325                 330                 335

aca ggg tac att gat aac gtg acc ctg gtt tca gcc cgc cct gtc ctt  1056
Thr Gly Tyr Ile Asp Asn Val Thr Leu Val Ser Ala Arg Pro Val Leu
            340                 345                 350

gga gcc cca gcc cct tgg gtt gaa cgt tgt gta tgc ctg ctg ggg tac  1104
Gly Ala Pro Ala Pro Trp Val Glu Arg Cys Val Cys Leu Leu Gly Tyr
        355                 360                 365

aag gga caa ttc tgc cag gaa tgt gct tct ggt tac aaa aga gat tcg  1152
Lys Gly Gln Phe Cys Gln Glu Cys Ala Ser Gly Tyr Lys Arg Asp Ser
    370                 375                 380

gca aga ttg ggc gct ttt ggc gcc tgt gtt ccc tgt aac tgc caa ggg  1200
Ala Arg Leu Gly Ala Phe Gly Ala Cys Val Pro Cys Asn Cys Gln Gly
385                 390                 395                 400

gag ggg gcc tgt gat cca gac acg gga gat tgc tac tcg ggg gac gag  1248
Glu Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr Ser Gly Asp Glu
                405                 410                 415

aat cct gac att gag tgt gct gac tgt ccc atc ggt ttc tac aat gac  1296
Asn Pro Asp Il  Glu Cys Ala Asp Cys Pro Ile Gly Phe Tyr Asn Asp
            420                 425                 430

cca cat gac ccc cgc agc tgc aag cca tgt ccc tgt cac aat ggg ttc  1344
Pro His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys His Asn Gly Phe
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        435                 440                 445

agc tgt tca gtg atg cct gag aca gag gag gtg gtg tgt aac aac tgt   1392
Ser Cys Ser Val Met Pro Glu Thr Glu Glu Val Val Cys Asn Asn Cys
    450                 455                 460

ccc cct ggg gtc aca ggt gcc cgc tgt gag ctc tgt gct gat ggc ttc   1440
Pro Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys Ala Asp Gly Phe
465                 470                 475                 480

ttt ggg gat ccc ttt ggg gaa cat ggc cca gtg agg cct tgt caa cgc   1488
Phe Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg Pro Cys Gln Arg
                485                 490                 495

tgc caa tgc aac aac aac gtg gac ccc aat gcc tct ggg aac tgt gac   1536
Cys Gln Cys Asn Asn Asn Val Asp Pro Asn Ala Ser Gly Asn Cys Asp
            500                 505                 510

cag ttg aca ggc aga tgc ttg aaa tgt atc tac aac acg gcc ggt gtc   1584
Gln Leu Thr Gly Arg Cys Leu Lys Cys Ile Tyr Asn Thr Ala Gly Val
        515                 520                 525

tac tgt gac cag tgc aaa gca ggt tac ttt gga gac cca ttg gct ccc   1632
Tyr Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp Pro Leu Ala Pro
    530                 535                 540

aac cca gca gac aag tgt cga gct tgc aac tgc agc ccc atg ggt gcg   1680
Asn Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Ser Pro Met Gly Ala
545                 550                 555                 560

gag cct gga gag tgt cga ggt gat ggc agc tgt gtt tgc aag cca ggc   1728
Glu Pro Gly Glu Cys Arg Gly Asp Gly Ser Cys Val Cys Lys Pro Gly
                565                 570                 575

ttt ggc gcc ttc aac tgt gat cac gca gcc cta acc agt tgt cct gct   1776
Phe Gly Ala Phe Asn Cys Asp His Ala Ala Leu Thr Ser Cys Pro Ala
            580                 585                 590

tgc tac aat caa gtg aag att cag atg gac cag ttt acc cag cag ctc   1824
Cys Tyr Asn Gln Val Lys Ile Gln Met Asp Gln Phe Thr Gln Gln Leu
        595                 600                 605

cag agc ctg gag gcc ctg gtt tca aag gct cag ggt ggt ggt ggt ggt   1872
Gln Ser Leu Glu Ala Leu Val Ser Lys Ala Gln Gly Gly Gly Gly Gly
    610                 615                 620

ggt aca gtc cca gtg cag ctg gaa ggc agg atc gag cag gct gag cag   1920
Gly Thr Val Pro Val Gln Leu Glu Gly Arg Ile Glu Gln Ala Glu Gln
625                 630                 635                 640

gcc ctt cag gac att ctg gga gaa gct cag att tca gaa ggg gca atg   1968
Ala Leu Gln Asp Ile Leu Gly Glu Ala Gln Ile Ser Glu Gly Ala Met
                645                 650                 655

aga gcc gtt gct gtc cgg ctg gcc aag gca agg agc caa gag aac gac   2016
Arg Ala Val Ala Val Arg Leu Ala Lys Ala Arg Ser Gln Glu Asn Asp
            660                 665                 670

tac aag acc cgc ctg gat gac ctc aag atg act gca gaa agg atc cgg   2064
Tyr Lys Thr Arg Leu Asp Asp Leu Lys Met Thr Ala Glu Arg Ile Arg
        675                 680                 685
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gcc ctg ggc agt cag cat cag aac aga gtt cag gat acg agc aga ctc   2112
Ala Leu Gly Ser Gln His Gln Asn Arg Val Gln Asp Thr Ser Arg Leu
    690                 695                 700

atc tct cag atg cgc ctg agt ctg gca gga agc gaa gct ctc ttg gaa   2160
Ile Ser Gln Met Arg Leu Ser Leu Ala Gly Ser Glu Ala Leu Leu Glu
705                 710                 715                 720

aac act aat atc cat tct tct gag cac tac gtg ggg ccg aat gat ttt   2208
Asn Thr Asn Ile His Ser Ser Glu His Tyr Val Gly Pro Asn Asp Phe
                725                 730                 735

aaa agt ctg gct cag gag gct aca aga aag gca gac agc cac gct gag   2256
Lys Ser Leu Ala Gln Glu Ala Thr Arg Lys Ala Asp Ser His Ala Glu
            740                 745                 750

tca gct aac gca atg aag caa cta gca agg gaa act gag gac tac tcc   2304
Ser Ala Asn Ala Met Lys Gln Leu Ala Arg Glu Thr Glu Asp Tyr Ser
        755                 760                 765

aaa caa gca ctt tca ttg gcc cgc aag ctc ttg agt gga gga ggc gga   2352
Lys Gln Ala Leu Ser Leu Ala Arg Lys Leu Leu Ser Gly Gly Gly Gly
    770                 775                 780

agt ggc tct tgg gac agc tcc gtg gta caa ggt ctt atg gga aaa tta   2400
Ser Gly Ser Trp Asp Ser Ser Val Val Gln Gly Leu Met Gly Lys Leu
785                 790                 795                 800

gag aaa acc aag tcc ctg agc cag cag ctg tca ttg gag ggc acc caa   2448
Glu Lys Thr Lys Ser Leu Ser Gln Gln Leu Ser Leu Glu Gly Thr Gln
                805                 810                 815

gcc gac att gaa gct gat agg tcg tat cag cac agt ctc cgc ctc ctg   2496
Ala Asp Ile Glu Ala Asp Arg Ser Tyr Gln His Ser Leu Arg Leu Leu
            820                 825                 830

gat tct gcc tct cag ctt cag gga gtc agt gat ctg tcc ttt cag gtg   2544
Asp Ser Ala Ser Gln Leu Gln Gly Val Ser Asp Leu Ser Phe Gln Val
        835                 840                 845

gaa gca aag agg atc aga caa aag gct gat tct ctc tca aac ctg gtg   2592
Glu Ala Lys Arg Ile Arg Gln Lys Ala Asp Ser Leu Ser Asn Leu Val
    850                 855                 860

acc aga caa acg gat gca ttc acg cgt gtg cga aac aat ctg ggg aac   2640
Thr Arg Gln Thr Asp Ala Phe Thr Arg Val Arg Asn Asn Leu Gly Asn
865                 870                 875                 880

tgg gaa aaa gaa aca cgg cag ctt tta cag act gga aag gat agg aga   2688
Trp Glu Lys Glu Thr Arg Gln Leu Leu Gln Thr Gly Lys Asp Arg Arg
                885                 890                 895

cag act tca gat cag ctg ctt tcc cgt gcc aac ctt gct aaa aac aga   2736
Gln Thr Ser Asp Gln Leu Leu Ser Arg Ala Asn Leu Ala Lys Asn Arg
            900                 905                 910

gcc caa gaa gcg cta agt atg ggc aat gcc act ttt tat gaa gtt gag   2784
Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr Phe Tyr Glu Val Glu
        915                 920                 925
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aac atc ctg aag aac ctc cga gag ttt gat ctg cag gtt gaa gac aga   2832
Asn Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu Gln Val Glu Asp Arg
    930                 935                 940

aaa gca gag gct gaa gag gcc atg aag aga ctc tcc tct att agc cag   2880
Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu Ser Ser Ile Ser Gln
945                 950                 955                 960

aag gtt gcg gat gcc agt gac aag acc cag caa gca gaa acg gcc ctg   2928
Lys Val Ala Asp Ala Ser Asp Lys Thr Gln Gln Ala Glu Thr Ala Leu
                965                 970                 975

ggg agc gcc act gcc gac acc caa cgg gca aag aac gca gct agg gag   2976
Gly Ser Ala Thr Ala Asp Thr Gln Arg Ala Lys Asn Ala Ala Arg Glu
            980                 985                 990

gcc ctg gag atc agc agc gag ata gag ctg gag ata ggg agt ctg aac   3024
Ala Leu Glu Ile Ser Ser Glu Ile Glu Leu Glu Ile Gly Ser Leu Asn
        995                1000                1005

ttg gaa gct aat gtg aca gca gat ggg gcc ttg gcc atg gag aaa ggg   3072
Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu Ala Met Glu Lys Gly
   1010                1015                1020

act gcc act ctg aag agc gag atg aga gag atg att gag ctg gcc aga   3120
Thr Ala Thr Leu Lys Ser Glu Met Arg Glu Met Ile Glu Leu Ala Arg
1025                1030                1035                1040

aag gag ctg gag ttt gac acg gat aag gac acg gtg cag ctg gtg att   3168
Lys Glu Leu Glu Phe Asp Thr Asp Lys Asp Thr Val Gln Leu Val Ile
                1045                1050                1055

act gaa gcc cag caa gct gat gcc aga gcc acg agt gcc gga gtt acc   3216
Thr Glu Ala Gln Gln Ala Asp Ala Arg Ala Thr Ser Ala Gly Val Thr
            1060                1065                1070

atc caa gac acr ctc aac aca ttg gac ggc atc cta cac ctc ata gac   3264
Ile Gln Asp Xaa Leu Asn Thr Leu Asp Gly Ile Leu His Leu Ile Asp
        1075                1080                1085

cag cct ggc agt gtg gat gaa gaa ggg atg atg cta tta gaa caa ggg   3312
Gln Pro Gly Ser Val Asp Glu Glu Gly Met Met Leu Leu Glu Gln Gly
   1090                1095                1100

ctt ttc caa gcc aag acc cag atc aac agt cga ctt cgg ccc ttg atg   3360
Leu Phe Gln Ala Lys Thr Gln Ile Asn Ser Arg Leu Arg Pro Leu Met
1105                1110                1115                1120

tct gac ctg gag gag agg gtg cgt cgg cag agg aac cac ctc cat ctg   3408
Ser Asp Leu Glu Glu Arg Val Arg Arg Gln Arg Asn His Leu His Leu
                1125                1130                1135

ctg gag act agc ata gat gga att ctt gct gat gtg aag aac ctg gag   3456
Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp Val Lys Asn Leu Glu
            1140                1145                1150

aac att cga gac aac ctg ccc cca ggc tgc tac aat acc caa gct ctt   3504
Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys Tyr Asn Thr Gln Ala Leu
        1155                1160                1165

gag caa cag tgaagttgtc atagagattt gtccactgtt gtgaaaggac           3553
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Glu Gln Gln
1170

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Leu Asn Cys Asn Asp Asn Thr Ala Gly Val His Cys Glu Arg Ser Arg
        35                  40                  45

Glu Gly Phe Tyr Gln His Gln Ser Lys Ser Arg Cys Leu Pro Cys Asn
    50                  55                  60

Cys His Ser Lys Gly Ser Leu Ser Ala Gly Cys Asp Asn Ser Gly Gln
65                  70                  75                  80

Cys Arg Cys Lys Pro Gly Val Thr Gly Gln Arg Cys Asp Gln Cys Gln
                85                  90                  95

Pro Gly Phe His Met Leu Thr Asp Ala Gly Cys Thr Arg Asp Gln Gly
            100                 105                 110

Gln Leu Asp Ser Lys Cys Asp Cys Asp Pro Ala Gly Ile Ser Gly Pro
        115                 120                 125

Cys Asp Ser Gly Arg Cys Val Cys Lys Pro Ala Val Thr Gly Glu Arg
    130                 135                 140

Cys Asp Arg Cys Arg Pro Arg Asp Tyr His Leu Asp Arg Ala Asn Pro
145                 150                 155                 160

Glu Gly Cys Thr Gln Cys Phe Cys Tyr Gly His Ser Ala Ser Cys His
                165                 170                 175

Ala Ser Ala Asp Phe Ser Val His Lys Ile Thr Ser Thr Phe Ser Gln
            180                 185                 190

Asp Val Asp Gly Trp Lys Ala Val Gln Arg Asn Gly Ala Pro Ala Lys
        195                 200                 205

Leu His Trp Ser Gln Arg His Arg Asp Val Phe Ser Ser Ala Arg Arg
    210                 215                 220

Ser Asp Pro Val Tyr Phe Val Ala Pro Ala Lys Phe Leu Gly Asn Gln
225                 230                 235                 240

Gln Val Ser Tyr Gly Gln Ser Leu Ser Phe Asp Tyr Arg Val Asp Arg
                245                 250                 255

Gly Gly Arg Gln Pro Ser Ala Tyr Asp Val Ile Leu Glu Gly Ala Gly
            260                 265                 270

Leu Gln Ile Arg Ala Pro Leu Met Ala Pro Gly Lys Thr Leu Pro Cys
        275                 280                 285

Gly Ile Thr Lys Thr Tyr Thr Phe Arg Leu Asn Glu His Pro Ser Ser
    290                 295                 300

His Trp Ser Pro Gln Leu Ser Tyr Phe Glu Tyr Arg Arg Leu Leu Arg
305                 310                 315                 320
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Asn Leu Thr Ala Leu Leu Met Ile Arg Ala Thr Tyr Gly Glu Tyr Ser
                325                 330                 335

Thr Gly Tyr Ile Asp Asn Val Thr Leu Val Ser Ala Arg Pro Val Leu
            340                 345                 350

Gly Ala Pro Ala Pro Trp Val Glu Arg Cys Val Cys Leu Leu Gly Tyr
        355                 360                 365

Lys Gly Gln Phe Cys Gln Glu Cys Ala Ser Gly Tyr Lys Arg Asp Ser
    370                 375                 380

Ala Arg Leu Gly Ala Phe Gly Ala Cys Val Pro Cys Asn Cys Gln Gly
385                 390                 395                 400

Glu Gly Ala Cys Asp Pro Asp Thr Gly Asp Cys Tyr Ser Gly Asp Glu
                405                 410                 415

Asn Pro Asp Ile Glu Cys Ala Asp Cys Pro Ile Gly Phe Tyr Asn Asp
            420                 425                 430

Pro His Asp Pro Arg Ser Cys Lys Pro Cys Pro Cys His Asn Gly Phe
        435                 440                 445

Ser Cys Ser Val Met Pro Glu Thr Glu Glu Val Val Cys Asn Asn Cys
    450                 455                 460

Pro Pro Gly Val Thr Gly Ala Arg Cys Glu Leu Cys Ala Asp Gly Phe
465                 470                 475                 480

Phe Gly Asp Pro Phe Gly Glu His Gly Pro Val Arg Pro Cys Gln Arg
                485                 490                 495

Cys Gln Cys Asn Asn Asn Val Asp Pro Asn Ala Ser Gly Asn Cys Asp
            500                 505                 510

Gln Leu Thr Gly Arg Cys Leu Lys Cys Ile Tyr Asn Thr Ala Gly Val
        515                 520                 525

Tyr Cys Asp Gln Cys Lys Ala Gly Tyr Phe Gly Asp Pro Leu Ala Pro
    530                 535                 540

Asn Pro Ala Asp Lys Cys Arg Ala Cys Asn Cys Ser Pro Met Gly Ala
545                 550                 555                 560

Glu Pro Gly Glu Cys Arg Gly Asp Gly Ser Cys Val Cys Lys Pro Gly
                565                 570                 575

Phe Gly Ala Phe Asn Cys Asp His Ala Ala Leu Thr Ser Cys Pro Ala
            580                 585                 590

Cys Tyr Asn Gln Val Lys Ile Gln Met Asp Gln Phe Thr Gln Gln Leu
        595                 600                 605

Gln Ser Leu Glu Ala Leu Val Ser Lys Ala Gln Gly Gly Gly Gly Gly
    610                 615                 620

Gly Thr Val Pro Val Gln Leu Glu Gly Arg Ile Glu Gln Ala Glu Gln
625                 630                 635                 640

Ala Leu Gln Asp Ile Leu Gly Glu Ala Gln Ile Ser Glu Gly Ala Met
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645 650 655

Arg Ala Val Ala Val Arg Leu Ala Lys Ala Arg Ser Gln Glu Asn Asp
660 665 670

Tyr Lys Thr Arg Leu Asp Asp Leu Lys Met Thr Ala Glu Arg Ile Arg
675 680 685

Ala Leu Gly Ser Gln His Gln Asn Arg Val Gln Asp Thr Ser Arg Leu
690 695 700

Ile Ser Gln Met Arg Leu Ser Leu Ala Gly Ser Glu Ala Leu Leu Glu
705 710 715 720

Asn Thr Asn Ile His Ser Ser Glu His Tyr Val Gly Pro Asn Asp Phe
725 730 735

Lys Ser Leu Ala Gln Glu Ala Thr Arg Lys Ala Asp Ser His Ala Glu
740 745 750

Ser Ala Asn Ala Met Lys Gln Leu Ala Arg Glu Thr Glu Asp Tyr Ser
755 760 765

Lys Gln Ala Leu Ser Leu Ala Arg Lys Leu Leu Ser Gly Gly Gly Gly
770 775 780

Ser Gly Ser Trp Asp Ser Ser Val Val Gln Gly Leu Met Gly Lys Leu
785 790 795 800

Glu Lys Thr Lys Ser Leu Ser Gln Gln Leu Ser Leu Glu Gly Thr Gln
805 810 815

Ala Asp Ile Glu Ala Asp Arg Ser Tyr Gln His Ser Leu Arg Leu Leu
820 825 830

Asp Ser Ala Ser Gln Leu Gln Gly Val Ser Asp Leu Ser Phe Gln Val
835 840 845

Glu Ala Lys Arg Ile Arg Gln Lys Ala Asp Ser Leu Ser Asn Leu Val
850 855 860

Thr Arg Gln Thr Asp Ala Phe Thr Arg Val Arg Asn Asn Leu Gly Asn
865 870 875 880

Trp Glu Lys Glu Thr Arg Gln Leu Leu Gln Thr Gly Lys Asp Arg Arg
885 890 895

Gln Thr Ser Asp Gln Leu Leu Ser Arg Ala Asn Leu Ala Lys Asn Arg
900 905 910

Ala Gln Glu Ala Leu Ser Met Gly Asn Ala Thr Phe Tyr Glu Val Glu
915 920 925

Asn Ile Leu Lys Asn Leu Arg Glu Phe Asp Leu Gln Val Glu Asp Arg
930 935 940

Lys Ala Glu Ala Glu Glu Ala Met Lys Arg Leu Ser Ser Ile Ser Gln
945 950 955 960

Lys Val Ala Asp Ala Ser Asp Lys Thr Gln Gln Ala Glu Thr Ala Leu
965 970 975

Gly Ser Ala Thr Ala Asp Thr Gln Arg Ala Lys Asn Ala Ala Arg Glu
980 985 990

Ala Leu Glu Ile Ser Ser Glu Ile Glu Leu Glu Ile Gly Ser Leu Asn
995 1000 1005

Leu Glu Ala Asn Val Thr Ala Asp Gly Ala Leu Ala Met Glu Lys Gly
1010 1015 1020

Thr Ala Thr Leu Lys Ser Glu Met Arg Glu Met Ile Glu Leu Ala Arg
1025 1030 1035 1040

Lys Glu Leu Glu Phe Asp Thr Asp Lys Asp Thr Val Gln Leu Val Ile
1045 1050 1055

Thr Glu Ala Gln Gln Ala Asp Ala Arg Ala Thr Ser Ala Gly Val Thr
1060 1065 1070

Ile Gln Asp Xaa Leu Asn Thr Leu Asp Gly Ile Leu His Leu Ile Asp
1075 1080 1085

Gln Pro Gly Ser Val Asp Glu Glu Gly Met Met Leu Leu Glu Gln Gly
1090 1095 1100

Leu Phe Gln Ala Lys Thr Gln Ile Asn Ser Arg Leu Arg Pro Leu Met
1105 1110 1115 1120

Ser Asp Leu Glu Glu Arg Val Arg Arg Gln Arg Asn His Leu His Leu
1125 1130 1135

Leu Glu Thr Ser Ile Asp Gly Ile Leu Ala Asp Val Lys Asn Leu Glu
1140 1145 1150

Asn Ile Arg Asp Asn Leu Pro Pro Gly Cys Tyr Asn Thr Gln Ala Leu
1155 1160 1165

Glu Gln Gln
1170